



NCC Pediatrics Continuity Clinic Curriculum: Enuresis *Faculty Guide*



Goals & Objectives: *Recognize and manage common developmental and behavioral conditions involving enuresis which generally do not require referral.*

- Identify and use the correct terms to describe pediatric urinary incontinence.
- Be able to take a thorough voiding and elimination history.
- Identify common comorbidities associated with NMSE.
- Describe and institute first line therapy for PMNE and NMSE.
- Describe indications for additional evaluation and referral to other professionals for evaluation or treatment of urinary incontinence.

Pre-Meeting Preparation:

Please read the following enclosures:

- “Nocturnal Enuresis: An Approach to Assessment and Treatment”(PIR, 2014)
- "Evaluation and Treatment of Nonmonosymptomatic Enuresis” (PIR, 2014)
- **“Show & Tell”:** Be prepared to discuss a “home remedy” for nocturnal enuresis (e.g. bedwetting alarms, watches, etc.). Research online.

Conference Agenda:

- Review Urinary Incontinence Quiz
- Complete Urinary Incontinence Cases
- **“Show & Tell”:** Discuss “home remedies” for PMNE.

Post-Conference: Board Review Q&A

Extra-Credit:

- [International Children’s Continence Society \(ICCS\) Terminology Report \(2006\)](#)
- [Enuresis: practical guidelines for primary care \(British Journal of General Practice, 2017\)](#)
- ["Management and treatment of nocturnal enuresis - an updated standardization document from the International Children's Continence Society" \(Journal of Pediatric Urology, 2020\)](#)
- [CAM Therapies for Enuresis \(PIR, 2009\)](#)—includes hypnosis, acupuncture, biofeedback
- [A Modified Biofeedback Program for Children with DSD \(J of Urology, 2001\)](#)
- [Evaluation and Management of Enuresis \(NEJM, 2009\)](#)— another review article
- [Bed-Wetting \(Enuresis\) Bright Futures Tool for Families](#)

Nocturnal Enuresis: An Approach to Assessment and Treatment

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Educational Gap

Although approximately 15% of children will have primary monosymptomatic nocturnal enuresis (PMNE) at age 6 years, only 1% to 2% of adolescents will continue to have wetting by the late teen years. Treating PMNE involves accurate diagnosis and an in-depth understanding of the multiple factors that cause children to wet. Failure to recognize causes of PMNE or nonmonosymptomatic nocturnal enuresis (also known as nonmonosymptomatic enuresis) will lead to treatment failure in many children.

Objectives After completing this article the reader should be able to:

1. Know the difference between primary monosymptomatic nocturnal enuresis (PMNE) and nonmonosymptomatic nocturnal enuresis.
2. Understand how to use a good history to guide treatment for PMNE.
3. Know the different treatments for PMNE as first-line therapy and understand why they are effective.
4. Be aware that children with secondary PMNE may not have an organic source for their wetting.
5. Recognize the psychological effect of PMNE on the child and family.

AUTHOR DISCLOSURE Drs Bayne and Skoog have disclosed no financial relationships relevant to this article. This commentary does contain a discussion of an unapproved/investigative use of a commercial product/device.

ABBREVIATIONS

EBC	expected bladder capacity
ICCS	International Children's Continence Society
ICS	International Continence Society
NE	nocturnal enuresis
NMNE	nonmonosymptomatic nocturnal enuresis
NP	nocturnal polyuria
PMNE	primary monosymptomatic nocturnal enuresis

CASE

Brittany is a 9-year-old girl seen in the pediatrician office for concerns about bedwetting. The family reports that the child has never been dry for more than a few nights in her entire life. The child is rather uncomfortable with the conversation, and the parents answer most of the questions. The family states they have "tried everything." They report trying to wake the child up at night to have the child void and did not have success with this. They state that the child is not allowed to drink any fluid within an hour before going to bed. The child voids immediately before going to sleep but seems to wet the bed 2 to 3 hours later.

The family states they are frustrated with the wetting because they are tired of doing laundry and that nighttime undergarments are becoming prohibitively expensive. They also worry about the child's development because she is

embarrassed to sleep at friends' houses for fear of wetting and being teased. When asked about bladder and bowel habits, the family states she is "normal" and has no daytime wetting incidents and no problems with constipation. Further questioning, however, reveals that the child's normal stooling pattern is one large bowel movement every 5 days that frequently clogs the toilet. The mother reports that this is normal for the child since toilet training. During a family history taking, the mother discloses that she wet the bed until age 12 years. The family reports the child is a profoundly deep sleeper who does not wake to alarms. They deny any other history of physical problems or any other traumatic physical or emotional events. They state that she has never had urinary tract infections in the past.

CLINICAL DESCRIPTION

Nocturnal enuresis (NE) is defined in accordance with the International Children's Continence Society (ICCS) as "intermittent nocturnal incontinence." (1) Primary monosymptomatic nocturnal enuresis (PMNE) is defined as lifelong continuous "enuresis without any other history of lower urinary tract symptoms and without a history of bladder dysfunction." (1) For all other children who do not fit these criteria, the broad term nonmonosymptomatic nocturnal enuresis (NMNE) is used. Children with NMNE may have a variety of different reasons for their enuresis, which should not be thought of as homogenous in cause or treatment. Reasons can include urinary tract infections, diurnal enuresis, and known anatomical or neurologic bladder dysfunction. A subset of children with NE who previously have had a dry period for 6 months or longer are characterized as having secondary NE. The need for differentiation of these terms is important because it is clear that treatment and success of treating these conditions vary greatly among the different categories. This review focuses on helping the clinician differentiate in a clinical setting the different subgroups of NE and initiate therapy appropriate for the subgroup identified.

PHYSIOLOGY

Children with PMNE can have a variety of different and overlapping physiologic variants that cause them to have incontinence. Central to PMNE is an inability of the child to awaken to the stimulation to void. Nearly every family will tell you that their child is a very heavy sleeper and that they do not wake to many types of physical or audible stimulation at night. Although sleep studies have been conflicting at finding a single type of sleep problem in these children, the lack of arousal is what characterizes these children and

separates them from children with nocturia in which the child awakens to void. It is therefore important to understand that difficulty with sleep arousal is central to virtually all children with all types of NE.

Another group of children with PMNE will have nocturnal polyuria (NP) as part of their condition. This condition is defined as urine production greater than 130% of the child's expected bladder capacity (EBC). The EBC is defined using the following equation: $EBC = 30 \text{ mL} + (\text{age in years} \times 30 \text{ mL})$. It is important to evaluate children with NP for conditions that raise the likelihood of nocturnal diuresis, such as sleep disordered breathing, heart abnormalities, metabolic conditions, and/or excess nocturnal fluid and solute intake. Sleep disordered breathing in particular has been the subject of many studies and is well known to cause or be associated with PMNE.

Some children with PMNE will have small bladder capacities. Bladder capacity can be determined by using the voiding diary and maximum voided volume to look for a pattern of frequent small volume voids during the day and should be considered especially likely when the maximum voided volume on the voiding diary is less than 50% of the EBC. Another group of children may have overactive bladders that do not manifest during the day or are not elicited by the history and voiding diary. Conditions in these children can be difficult to diagnose without using urodynamics, but prior studies have clearly found that this can be an important reason for the PMNE in a small subset of children.

Although sleep arousal abnormalities, NP, sleep disordered breathing, small bladder capacity, and overactive bladder can be independent causes of PMNE, in most children these factors can occur in combination, with many children having 2 or even 3 of these factors. In many cases, there is a strong genetic or familial cause that can further complicate this and can be elicited by taking a thorough family history. In our case presentation, it would seem that Brittany has a clear genetic component to her enuresis, sleep arousal difficulty, and possibly NP complicated by constipation.

EPIDEMIOLOGY

NE is a common condition in early childhood that decreases in prevalence as children approach adolescence. NE is ubiquitous in the newborn and is part of the infantile voiding pattern. A total of 10% to 15% of children will still wet the bed by age 6 years. Up to 15% of children will outgrow the condition annually in the teenage years so that only 1% to 2% of people will still have PMNE into adulthood. (2)(3) The condition is more common among boys and in children with a first-degree relative with a history of PMNE. If one parent

has a history of PMNE, then up to half of their children will have it. If both parents had PMNE, then up to three-fourths of the children will have it. PMNE is seen more commonly in children with attention-deficit/hyperactivity disorder, which frequently represent challenging cases for treatment.

EVALUATION OF NE

The evaluation of the child with NE starts with a complete history and physical examination. Although a complete history is ideal, not every pediatrician has the time on the initial visit to address all the clinical history details associated with enuresis. A rapid screening series of questions can accurately categorize most children with NE. These questions are listed in Table 1. The main goal of the questions is to accurately characterize the type of NE that should in turn guide a more efficacious treatment plan.

If the pediatrician has the time to perform a more thorough history, then the following components should be addressed. How many nights per week does the child wet? What is the perceived volume of nocturnal leakage? What is the child's bedtime routine, and what is the evening fluid consumption? Has the child been dry for 6 months or longer? Does the child have a history of urine control problems during the day, including daytime incontinence, significant urgency or frequency, or urinary tract infections? Although classic voiding dysfunction that involves abnormal pelvic floor muscle control during voiding is difficult to discern on a history, certain specific questions focused on posturing or other physical behaviors to suppress urination should be elicited. A history of straining to urinate, urinary retention, feeling of incomplete emptying, and/or a start-stop pattern of voiding should raise suspicion for an underlying voiding problem.

Constipation is commonly associated with NE, and many families may not be aware that their child is constipated. Directed questions about fecal elimination habits must be elicited. How often does a child have bowel movements? Are

the bowel movements associated with pain or bleeding? Does the child have stools of large enough caliber to clog the toilet? Does the child have unintentional fecal voiding? Because the visit is focused on the urination problem, some families may not be aware that their child has concomitant constipation, and the recognition and treatment of constipation are important if the child hopes to resolve the NE.

Does the child have sleep apnea, snoring, or other types of sleep disordered breathing? Is there a family history of NE? At what age did the affected relative resolve his/her enuresis? Many parents will tell you they have tried everything as in the case study, but it is important to ask specifically what has been tried and what the outcome was. It is important to identify significant psychological stressors in the child's life and specific questions about birth of new siblings, death of relatives, trouble in school, abuse, divorce, and other major life stressors should be asked.

The final questions should focus on the degree to which the child is interested in treatment and the degree to which the child is bothered by the problem. The family and not the child are frequently most affected by NE, and treatment that involves behavior modification is unlikely to be successful when the child is not motivated to participate. The greatest effect to the child with PMNE is psychological, and it is important to ask specifically whether the NE affects the child. Does it limit going to friends' houses or camps? Does it cause the child social isolation? Does the child feel that there is something wrong with him/her? Children with NE should never be punished for the incontinence because it is not consciously controlled and punitive therapy has no basis in the treatment of this condition.

The physical examination of a child with NE should focus on the identification of findings that would identify underlying disorders in children with NMNE. A genital examination should focus on identifying labial adhesions in girls and meatal stenosis in boys. Girls with continuous leaking of fluid from the vagina or perineum should make the

TABLE 1. **Rapid Screen to Determine Type of Enuresis**

QUESTION	IF RESPONSE IS POSITIVE, THEN CONSIDER
Previously dry for 6 months	NMNE or SNE
Associated with daytime urine control issues	NMNE
Constipation or fecal soiling	NMNE
Severe recent stress	SNE
If responses to all above questions are negative, then consider	MNE

MNE=monosymptomatic nocturnal enuresis; NMNE=nonmonosymptomatic nocturnal enuresis; SNE=secondary nocturnal enuresis.

examiner concerned for an ectopic ureter as the source of the enuresis. The clinician should be able to identify the anus, vaginal opening, and urethral opening. If the vaginal and/or urethral opening is not seen, then labial adhesions might be present. Checking the skin of the genital area may help identify children who have skin changes from chronic wetness or irritation. It is important to check the underwear of the child to assess for wetness and stool streaking. Stool around the anus may be a product of poor wiping but might be indicative of encopresis or constipation. Perianal tears or fissures may suggest longstanding constipation.

A neurologic examination checking for perineal sensation will help identify underlying spinal cord disease. It is also important to closely examine the sacrum and lumbar spine. Sacral dimples, tufts of hair over the midline, and abnormal or asymmetric gluteal cleft should raise the examiner's suspicion of an underlying spinal cord problem, such as tethered cord, cord lipoma, or persistent dural sinus. An abdominal examination to check for a palpable bladder and for significant palpable stool in the left lower quadrant should be performed. When indicated by the history, an evaluation of the oropharynx should be performed to determine the location and size of the tonsils.

In all children with NE, according to the International Continence Society (ICS), the only mandatory screening laboratory should be urinalysis. (4) This is useful to identify renal disease in cases where proteinuria or hematuria is present and to rule out urinary infection as the cause of the NE. Occult cystitis may not be elicited by a history or physical examination, and a urinalysis should be able to detect this. If the child has a low specific gravity, then diabetes insipidus or other causes of polyuria should be considered.

In most cases, it is appropriate for the pediatrician and certainly the enuresis specialist to have the family complete an elimination diary. This diary should consist of a stool and bladder diary that documents the timing and volume of voids, number and type of stools during the day, and characterization and documentation of any urine or stool leakage. A diary should also be kept to document fluid intake. Documentation of the volume of nocturnal urine production by weighing nighttime undergarments or sheets should be attempted in hopes of identifying children with NP. This is difficult and rarely achieved or performed correctly. For the voiding diary, it is important for families to have a urinal or receptacle to measure the volume of the voids. Measurement of the urine volume outside the house is not recommended, but on a weekend when the family is at home it is useful to record the actual voided volume for the day and for each void. By establishing the child's maximum voided volume during the day, it gives an estimate of the child's bladder capacity.

This should be mandatory for all specialist evaluations of children with NE and especially those who have had treatment failure because this helps identify children who have small bladder capacity or excessive urine production. The fluid intake will help identify children with increased solute or fluid intake. Although not mandatory, recording the type of fluids the child is drinking can be important, especially if the child is consuming large volumes of caffeinated beverages because these may have a diuretic effect and create overactivity in the bladder. These types of beverages should be reduced or eliminated from the child's diet and especially eliminated before bed.

TREATMENT OF PMNE

Lifestyle

Treatment for PMNE depends greatly on factors identified in the history, physical examination, and elimination diaries. The ICCS outlined 2 first-line treatments for children with PMNE. The 2 treatments are desmopressin and the bed alarm. Each of these 2 treatments is supported by Level I evidence from randomized clinical trials and has been subjected to Cochrane reviews and should be initiated in children only after careful evaluation to eliminate other psychological or physical causes of NE. Although the 2 first-line treatments deserve careful discussion, there are a few guidelines to which all children with PMNE should adhere. All children with PMNE should attempt to limit their fluid and solute consumption during the evening hours only. It is important that children have adequate hydration during the day and at school so that excessive thirst or dehydration is not occurring by the end of the day, causing the child to need more fluid intake in the evening. Some children with bladder dysfunction or bathroom-related anxieties will limit their fluid intake at school and will consume most of their fluid for the day in the few hours before bed. This is problematic in that it makes the NE difficult to treat and covers up what may be a more significant daytime problem. A good rule of thumb is for the child to consume two thirds of their fluid before the end of the school day and then one-third of the fluid in the evening with no further fluid consumption in the last hour before bed. This plan ensures adequate daytime hydration and attempts to limit NP. For children with PMNE who have activities in the evening, such as sports or other physical activities, this routine can be tricky to accomplish. In general, limiting fluids should never supersede adequate hydration for a child. Children with PMNE should try to establish a stable and reliable bedtime routine. Stable sleep patterns that result in a well-rested child lessen situations of excessive fatigue where the child is more difficult to arouse to internal and external

stimulation. Finally, all children with PMNE should empty their bladder before going to sleep and should void again whenever they wake up at night as well. (2)(4)(7)(8)

The Alarm

The bedwetting alarm is 1 of 2 first-line interventions recommended by the ICCS for children with PMNE. (4) The bedwetting alarm is focused on altering the sleep arousal associated with voiding. Bed alarms can be effective using vibratory or auditory stimuli or both. In the authors' experience, the auditory alarms seem most effective because they alert the parents that the child has had a wetting event. Use of the alarm can involve the whole family. The alarm should be used consistently, and the child should be motivated to participate. The child may not awaken initially, so the parents should awaken the child when the alarm sounds. On awakening, the child should void in the bathroom and then assist their parents in changing their bedding before returning to bed. Use of the alarm can take many weeks to months to work. Although the exact mechanism of action of the alarm is not completely understood, the effects are not limited to sleep arousal alone. Many studies have found that bladder capacity at night increases with use of the alarm.

Of all the treatments for PMNE, the alarm is one of the most effective and has the best long-term cure rate. The alarm is the most durable treatment for children with PMNE. In children who have a good response while using the alarm, only a small percentage will have a relapse after discontinued use of the alarm. In a Cochrane Review of randomized trials, the alarm was associated with a positive response in up to two-thirds of patients. (9) A number of clinical guidelines from multiple countries recommend the alarm as first-line therapy. (2)(4)(7) According to the ICCS, the alarm should be tried for at least 2 to 3 months. If treatment is effective, then it is recommended to continue use of the alarm until at least 14 consecutive dry nights are achieved. If a relapse occurs, then a second trial of alarm therapy can be successfully used.

Desmopressin

Desmopressin is a vasopressin analogue that reduces the amount of urine produced at night. In a Cochrane Review of clinical trials, the use of desmopressin compared with placebo desmopressin led to dryness in 20% to 30%, and up to 40% of patients may have had a partial response. (2)(5) Desmopressin is particularly useful in children with NP. Although success with desmopressin is favorable, the relapse rate is higher than the alarm but wide ranging in the literature.

Families and patients should be counseled about the risk of hyponatremia associated with desmopressin. It is especially important to limit fluid intake at night when the medication is used. The risk of this complication is higher when the nasal spray is used. Because of this, the nasal spray is not recommended, and instead the oral preparation is preferred. A number of guidelines recommend limiting fluid consumption starting 1 hour before the medication is given and until the child wakes the next morning. The ICCS guidelines recommend limiting a child's evening intake to 200 mL. (4) The tablet dose ranges from 0.2 to 0.4 mg. The effect is usually seen shortly after starting use of the medication. Long-term use does not seem to be harmful, but many of the guidelines suggest withdrawal of the medication every 3 months as a way to check and see whether the child still needs desmopressin and to allow the child a brief period of not taking the medication. (4)(7)

Anticholinergics

Anticholinergics, oxybutynin and tolterodine, are not recommended first line treatment in any child with PMNE. There are certain specific instances when their use is justified and recommended. In children with small bladder capacity by voiding diary or history consistent with over-activity anticholinergics can be very effective as adjunctive therapy. The ICCS recommends its use only after DDAVP or the alarm therapy has failed. (4) There is randomized data showing that combination therapy with DDAVP and anticholinergic medication is superior to DDAVP alone in children with small bladder volumes and refractory enuresis. Recommended starting dose is 5mg of oxybutynin or 2 mg of tolterodine at bedtime. Since these medications decrease bladder activity it is important for children to be instructed in proper voiding techniques and frequency to limit post-void residual urine volume. A common side effect of anticholinergic medications is constipation and this may also impact the success of this therapy. Any child being treated with anticholinergic medication should be routinely monitored for constipation and treated when indicated.

Imipramine

Imipramine and other tricyclic antidepressants have been used in children with PMNE with reasonable success. They are not considered first-line agents based more on their risk than on their benefit. Their benefit has been established with many clinical trials, and a Cochrane Review found that approximately 20% of children will achieve dryness (similar to desmopressin). (10) The relapse rate for imipramine is high, with more than 90% of children experiencing PMNE recurrence when use of the medication is stopped. The dose

TABLE 2. Potential Reasons for Treatment Failure of Enuresis

CAUSE	NEXT STEP
Constipation or retained fecal burden	Bowel regimen
Occult voiding dysfunction	Behavioral therapy, postvoid residual volume, uroflowmetry
Treatment compliance failure	Family goal discussion and assessment of child's interest in participation
Neurologic condition	Detailed neurologic examination and consider lumbar magnetic resonance imaging
Psychological stressors	Psychological evaluation and counseling as needed
Metabolic concerns	Laboratory evaluation and consider endocrine referral
Sleep disorders	Sleep laboratory referral with polysomnography
Sleep disordered breathing	Sleep specialist referral or otolaryngologist referral

of imipramine is 25 to 50 mg at bedtime. Similar to desmopressin, the medication should be tapered or withdrawn every 3 months to check for resolution of the PMNE and to allow the child some time not taking the medication.

Imipramine has seen a decrease in use secondary to its safety concerns. Imipramine has been found to have a risk of QT prolongation in children, and a careful cardiac history for the child and the family should be obtained before starting use of the medication. Sudden cardiac death in a family history should raise concern for QT prolongation. Imipramine has other adverse effects, but these are milder and less serious. Some data suggest that imipramine might be useful in children with refractory PMNE and attention-

deficit/hyperactivity disorder in whom first-line treatments with either desmopressin or alarm therapy have failed. Current guidelines suggest that use of imipramine be limited to specialty centers with extensive experience treating PMNE. (4)

Other Treatments

A recent Cochrane review of alternative therapy, including hypnosis and acupuncture, had insufficient data to recommend their use in children with PMNE based mostly on the poor quality of the data available for analysis. (11)(12) It is not recommended that these therapies be tried as first-line therapy but may be incorporated in a more complex treatment

TABLE 3. Possible Treatment Protocols in MNE

TYPE OF MNE	TREATMENT
All cases	Limit fluids before bed (≤200 mL)
	Void before bed
	Regular sleep and wake schedule
Classic PMNE	Alarm (first)
	Desmopressin (second)
Nocturnal polyuria	Desmopressin
Sleep disordered breathing	Sleep study or referral to an otorhinolaryngologist
Small bladder capacity	Alarm
Overactive bladder (suspected)	Desmopressin and oxybutynin
	Alarm and oxybutynin
Small bladder and nocturnal polyuria	Desmopressin and alarm (consider oxybutynin as well)

MNE=monosymptomatic nocturnal enuresis; PMNE=primary monosymptomatic nocturnal enuresis.

plan for refractory children. A recent review summarized the available data and found that hypnotherapy in a case series could have effects similar to imipramine with a lower relapse rate. (13) Hypnotherapy involves placing the child in a trance-like state and making a suggestion to the child to awaken when he/she needs to void at night. Optimal number of treatments and duration of treatment are not known.

Acupuncture data vary greatly in the literature, with few quality randomized trials allowing for direct comparison to other forms of treatment. In the limited number of series available, success rates have ranged widely, with some reported success rates higher than with the alarm therapy and some with rates far below. These treatments, although promising, need more data from quality randomized trials before recommending them for use in children with PMNE.

REFRACTORY CASES OF NE

For children with therapy-resistant NE, it is important for the primary care physician or specialist to investigate possible causes for this. Table 2 outlines potential causes of treatment failure and offers suggestions for the next step in management. Because constipation is difficult to diagnose, it can be a frequent cause of treatment failure and deserves special mention. A number of studies have reported that in children with both constipation and PMNE, a significant number would resolve their PMNE through treatment of constipation alone. Constipation may limit the bladder's ability to expand and contribute to bladder overactivity, thereby decreasing the likelihood of success with first-line treatments for PMNE. Direct questioning about type, size, and frequency of stool and possibly using a stool diary should be encouraged in these children with refractory NE.

Secondary Enuresis

Secondary enuresis exists when the child with bedwetting has been previously dry for more than 6 months consecutively. The evaluation and management are essentially the same as for any child with a history of PMNE, but special attention should focus on possible underlying psychiatric or emotional problems. (14) Questions directed toward major life events (birth of a sibling, death of a relative, parental divorce, or a recent move), school problems, or psychologically stressful situations should be investigated.

NMNE

For children with NMNE the ICCS recommends that the daytime elimination problem, either voiding or stooling, be addressed before starting any therapy for the NE component. (4) Typically, this involves regimented stooling and voiding

patterns and may involve referral to a specialist. These children may benefit greatly from urotherapy (biofeedback, timed voiding, pelvic floor training, double voiding, and/or anticholinergic medications) and behavioral modification and frequently require renal bladder ultrasonography, non-invasive uroflowmetry, and measurement of a postvoid residual. Although this article makes the clear distinction between PMNE and NMNE, the reality of clinical diagnosis is less clear. There is likely a large overlap between these conditions, and only by in-depth evaluation can some of these subtle voiding and stooling conditions be elicited.

Summary

- On the basis of strong evidence, although primary monosymptomatic nocturnal enuresis (PMNE) is common and most children will outgrow the condition spontaneously, the psychological effect to the child can be significant and represents the main reason for treatment of these children.
- On the basis of international consensus panels, treatment of PMNE should be targeted toward the specific type of bedwetting patterns the child has, using bladder diary, sleep history, and daytime elimination concerns as a guide (Table 3).
- On the basis of international consensus panels, it is important for the primary care physician to be able to differentiate children with PMNE from children with nonmonosymptomatic nocturnal enuresis (NMNE) and secondary nocturnal enuresis.
- On the basis of international consensus panels, children with NMNE should have their underlying voiding or stool problem addressed before initiation of therapy for the nocturnal enuresis.
- On the basis of strong evidence, both the bedwetting alarm and desmopressin are considered first-line therapy for children with PMNE.

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Parent Resources from the AAP at HealthyChildren.org

- English: <http://www.healthychildren.org/English/health-issues/conditions/genitourinary-tract/Pages/Nocturnal-Enuresis-in-Teens.aspx>
- Spanish: <http://www.healthychildren.org/spanish/health-issues/conditions/genitourinary-tract/paginas/nocturnal-enuresis-in-teens.aspx>

Evaluation and Treatment of Nonmonosymptomatic Enuresis

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Practice Gap

Among children 7½ years old with enuresis, 31.6% will have evidence of concomitant lower urinary tract (LUT) dysfunction. This nonmonosymptomatic enuresis represents a separate clinical entity from monosymptomatic enuresis and requires addressing the LUT dysfunction before enuresis treatment to avoid high treatment failure rates.

Butler RJ, Golding J, Northstone K. Nocturnal enuresis at 7.5 years old: prevalence and analysis of clinical signs. *BJU Int.* 2005;96(3):404–410.

Objectives After reading this review, the practitioner should be able to:

1. Identify and use correct terms to accurately describe pediatric urinary incontinence.
2. Take a thorough voiding and elimination history and differentiate between monosymptomatic and nonmonosymptomatic enuresis (NMSE)
3. Identify common comorbid conditions associated with NMSE.
4. Describe and institute first-line therapy for monosymptomatic enuresis and NMSE.
5. Recognize children with anatomical findings or children with refractory responses to first-line treatments that necessitate a specialist referral for lower urinary tract dysfunction and/or enuresis.

BACKGROUND AND DEFINITIONS

Parental concerns about urinary continence in children are commonly cited worries at primary pediatric appointments. A basic understanding of the classification and treatment of urinary incontinence and enuresis in otherwise neurologically normal children is thus essential for the practicing pediatrician. Many times, first-line behavioral modification techniques for encouraging proper bladder and bowel habits can be successful in primarily treating urinary symptoms without the need for referral to a subspecialist. The key to management

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ABBREVIATIONS

BBD bladder-bowel dysfunction
LUT lower urinary tract
MSE monosymptomatic enuresis
NMSE nonmonosymptomatic enuresis

lies in accurately characterizing and classifying the type of incontinence and providing targeted medical therapy for each situation. Enuresis without other lower urinary tract (LUT) symptoms (nocturia excluded) and without bladder dysfunction is defined as *monosymptomatic enuresis* (MSE). Children with enuresis and any LUT symptoms are said to have *nonmonosymptomatic enuresis* (NMSE). For the purposes of this review, we focus on NMSE. Formerly termed *diurnal enuresis*, this term has been reclassified to NMSE by the International Children's Continence Society standardization documents. (1)(2)

Before delving further into the treatment of NMSE, a brief review of common terms that pertain to pediatric LUT dysfunction is essential to establish accurate communication among pediatric health care professionals. In addition, common terms assist in the determination of the appropriate characterization of the LUT function in tailoring treatment of these children.

Urinary incontinence is the involuntary leakage of urine. This can be either continuous or intermittent and can occur during the day or at night.

Continuous incontinence usually has an associated anatomic origin, such as an ectopic ureter, whereas **intermittent incontinence** usually has associated functional disturbances in the voiding process.

Daytime incontinence (usually simply referred to as incontinence) is involuntary leakage of urine during waking hours.

Enuresis refers to intermittent incontinence that happens while the child is asleep. This most often occurs at night but can also happen with daytime sleep, such as naps.

Other common urinary symptoms in children include **increased frequency** (voiding ≥ 8 times daily), **decreased frequency** (voiding ≤ 3 times daily), **dysuria** (pain or discomfort with urination), **hesitancy** (difficulty in initiating a void), **intermittency** (a stream that stops and starts during the micturition process), and **urgency** (sudden, unexpected strong desire to urinate). LUT dysfunction in a child with bowel function disturbances, such as constipation, encopresis, or fecal incontinence, represents a combined pathophysiologic condition termed **bladder-bowel dysfunction (BBD)**. (1)(2)

Generally, urinary incontinence is not considered pathologic until a child reaches age 5 years as characterized by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, and the *International Classification of Diseases, 10th Revision*. (3)(4) Of course, there is variability in the maturational aspect of LUT function, and many children may have voluntary control over LUT function before age 5 years.

EPIDEMIOLOGY, PATHOPHYSIOLOGY, AND TARGETS OF THERAPY

The British Avon Longitudinal Study of Parents and Children Study, the only prospective longitudinal study of voiding habits in more than 8000 children, found that approximately 15% of all children 7½ years old experience enuresis, or nighttime wetting. (5) For many children, this is a solitary event (termed MSE); however, the prevalence of daytime urinary symptoms increases with the frequency of enuresis. Roughly one-third of children with 2 or more nights of enuresis per week will also have daytime urinary symptoms and thus have NMSE. (6)

MSE is thought to arise from 3 primary physiologic disturbances that involve the kidney, brain, and bladder. First, there is nocturnal polyuria present in a subset of children, diminished sleep arousal in another, and nocturnal bladder overactivity or reduced nocturnal bladder capacity in a final cohort. Treatments of enuresis are traditionally based on the predominant component of these 3 physiologic processes. (7) There may also be overlap of these 3 physiologic causes of enuresis, necessitating combination therapy. In children with NMSE, there is concomitant LUT dysfunction that renders traditional therapies ineffective. Children with NMSE will often have bowel issues, and constipation is a known contributor for LUT dysfunction. **Thus, treatment of NMSE is based on addressing any BBD, which often results in improvement and sometimes resolution of the accompanying enuresis.** (8)

COMORBID CONDITIONS

Although less frequent than other functional elimination disorders, children with enuresis have approximately a 20% to 30% incidence of comorbid behavioral conditions, such as attention-deficit/hyperactivity disorder, oppositional defiant disorder, and conduct disorder. (9) These comorbid conditions should be addressed in conjunction with the enuresis to optimize treatment.

EVALUATION OF THE PATIENT WITH ENURESIS

History

The primary evaluation approach for evaluating enuresis in a pediatric patient is a thorough elimination history. Of particular importance is the clarification of the LUT dysfunction symptoms (eg, frequency of enuresis, the presence or absence of daytime urinary symptoms, presence of comorbid behavioral issues or constipation, and whether the enuresis has been continuous since toilet training or is

a new development after an initial period of continence). Children who begin having enuresis after a dry period of greater than 6 months (termed *secondary enuresis*) should be questioned about any responsible social stressors.

An elimination history should include information on the typical daily bladder- and bowel-emptying habits of the child. When possible, having parents keep a bladder and bowel diary for a 1-week period before the appointment can improve the accuracy of the assessment of the child's voiding and stooling patterns. A *complete bladder diary* consists of a 7-night recording of incontinence episodes and nighttime urine volume measurements and is used to evaluate enuresis. A *48-hour daytime frequency and volume chart* is used to evaluate LUT dysfunction. This detailed 48-hour assessment provides information on the fluid intake volumes, the voided volumes, and the presence or absence of incontinence and is useful in differentiating idiopathic urinary frequency from polyuria. This 48-hour daytime frequency and volume chart is usually kept during a week-end to make adherence easier for the family. **Many parents and children are unaware of LUT dysfunction on routine questioning, and symptoms may not be apparent without an adequate voiding history and diary.**

Another relevant question is the posture of the child while voiding. Young girls will often slump while sitting on the toilet without an upright posture or inadequately spread their legs apart during voiding. Petite girls may also fall through the toilet seat, preventing good egress of urine from the urethra. A footstool at the base of the toilet or having the child sit astride and face the toilet will allow them to use better posture and correct these problems. Finally, some children will exhibit leg crossing, squatting on the floor, or sitting on the edge of a chair to compress their perineum. These posturing maneuvers are compensatory responses to counter bladder spasms when the bladder is too full or overactive and the perineal pressure inhibits bladder contraction through the sacral reflex arc.

Prior documentation of urinary tract infection suggests some component of urinary stasis or incomplete emptying. Many children with LUT dysfunction may experience symptoms consistent with cystitis, such as dysuria, urinary frequency, and suprapubic pain or discomfort related to voiding, although urine culture is sterile. These children may have urinalysis findings of pyuria, hematuria, and amorphous debris that reflect chronic inflammation and irritation in response to urinary stasis. Children with enuresis who have had a history of cystitis or recurrent cystitis symptoms should be considered to have LUT dysfunction and should be treated as having NMSE rather than MSE.

Evaluation should also include a brief screening for new neurologic symptoms, such as a change in coordination or gait disturbances. Finally, it is also helpful to discuss voiding problems sensitively and openly with the parents and child to remove any stigma associated with any LUT dysfunction.

Physical Examination

A general physical examination should be performed for children who present with NMSE, including a genital examination. The pertinent findings for each portion of the examination are summarized below.

Examination of the abdomen should include assessment of any abdominal distention or bloating that might indicate underlying bowel dysfunction. Palpation should be performed, looking for any palpable abdominal masses or abdominal tenderness, especially the suprapubic region, which would suggest urinary retention. In smaller children with severe constipation, the sigmoid colon may be palpable in the left lower quadrant.

A neurologic examination should include an assessment of strength, sensation, and coordination of all extremities. Careful examination of the spine through inspection and palpation is important to exclude underlying occult neurologic conditions. Any bony abnormalities of the vertebrae or sacrum should be further investigated. Any central cutaneous abnormalities overlying the spine, such as a sacral dimple, gluteal cleft, or lipoma or hair tuft, should also prompt further consideration for investigation because these may signify occult spinal cord anomalies (eg, tethered cord, diastematomyelia, and lumbosacral defects).

Pertinent findings on genital examination include appearance of the external genitalia and presence of irritation or dampness of the underwear or perineum. Blood or a bulge at the urethral meatus may indicate a urethral polyp or anatomical cause for voiding symptoms. The vaginal introitus should be examined for pooling of urine or irritation. If there is continuous incontinence, examination of the introitus for an ectopic ureteral orifice should be performed. If a patient has chronic irritation of the genitalia and perineum, skin changes or labial hypertrophy may be observed. (7)

Ultrasonography and Uroflow

Although not within the scope of practice for primary care practitioners, noninvasive urodynamic measurements determined by an office pelvic ultrasonography and uroflow can assist in differentiating MSE from NMSE and are commonly used in pediatric urology consultations. Findings on prevoid and postvoid ultrasonography consistent with NMSE include an enlarged bladder capacity (>150% expected for the child's age), incomplete emptying (a postvoid

residual of >10% expected capacity), or a thickened bladder wall suggestive of increased workload on the bladder muscle (detrusor muscle) during emptying due to increased bladder outlet resistance and pelvic floor muscle tone. A rectal diameter greater than 30 mm in a child without the urge to defecate is suggestive of concomitant bowel dysfunction. Uroflowmetry allows the pediatric specialist to assess the urinary flow pattern, and the shape of the flow curve may indicate underlying disease because shape is determined by detrusor contractility and influenced by abdominal straining, coordination with the bladder outlet musculature, and any distal anatomical obstruction. The urinary flow curve of a healthy child is bell-shaped, and other flow patterns are suggestive of underlying LUT dysfunction and NMSE. (10)(11)

THErapy

Therapy for NMSE is based on the following principles.

1. Address any underlying constipation or fecal incontinence.
2. Address any LUT dysfunction and daytime voiding symptoms.
3. Address any comorbid behavioral conditions.
4. If enuresis is still present after addressing the above, institute standard therapies for MSE.

Although treatment of severe fecal incontinence and behavioral conditions are outside the scope of this article, many validated techniques exist for treatment of these comorbidities that may accompany enuresis. We review these treatment concepts in further detail.

CONSTIPATION

Even in children without pathologic constipation or fecal incontinence, addressing subclinical constipation can result in marked improvement in LUT dysfunction. Multiple observational studies report improvement of urinary tract dysfunction in 60% to 90% of children treated for underlying constipation. (12) Although increased dietary fiber and adequate hydration are the first-line therapy for constipation, many children will require further treatment. Second-line therapy is typically a fiber supplement and an osmotic laxative, such as polyethylene glycol, titrated to give a smooth, daily bowel movement that does not require straining or cause pain. A pictorial scale, such as the Bristol stool scale, can be useful in communicating accurately with families regarding the child's bowel habits. (13) Severe cases of constipation may require hospital admission and fecal disimpaction. This should only be undertaken after consultation with a gastroenterologist, and the children should be evaluated for possible pathologic causes of bowel dysfunction,

such as underlying neurologic conditions or Hirschsprung disease. (12)

BEHAVIORAL CONDITIONS

Addressing behavioral comorbidities in conjunction with LUT dysfunction should be in accordance with existing therapeutic approaches. Although some conditions may be amenable to management in a primary setting (such as stimulant medication and counseling for attention-deficit/hyperactivity disorder), many may require further expertise, such as referral to a psychiatrist or psychologist. (9)

UROTherapy

Urotherapy is conservative-based therapy and the mainstay of treatment for LUT dysfunction. The hallmark of urotherapy is parental and patient education on normal elimination habits and institution of a structured behavioral program designed to improve bladder and bowel function. In our practice, we routinely use an educational handout for parents with information about managing constipation and encouraging good posture and voiding habits. Both the child and parents keep diaries to monitor and record the elimination patterns. For the child, the voiding diary is also a reward chart for children to color or place stickers for each attempted void. Parents record a week-long elimination diary about their child's elimination patterns and any symptoms of BBD during weeks 1 (baseline), 6, and 12 of the program. These scheduled time points allow for accurate assessment of the child's progress from the behavioral modification and indicate need for any further follow-up or additional treatment. For most children with LUT dysfunction, this behavioral modification program is the only necessary treatment. When children are refractory to standard urotherapy, evaluation for possible underlying neurologic abnormalities and referral to a pediatric urologist should be considered before instituting more advanced therapeutic techniques.

ADVANCED UROTherapy TECHNIQUES

Advanced urotherapy techniques include biofeedback techniques for assessing pelvic floor musculature and pelvic floor musculature physiotherapy. In addition, neurostimulation with sacral transcutaneous electrical nerve stimulation and posterior tibial nerve stimulation are alternative methods of modulating the sacral nerves responsible for control of the pelvic floor. These advanced techniques are generally performed by pediatric subspecialists and involve specialized

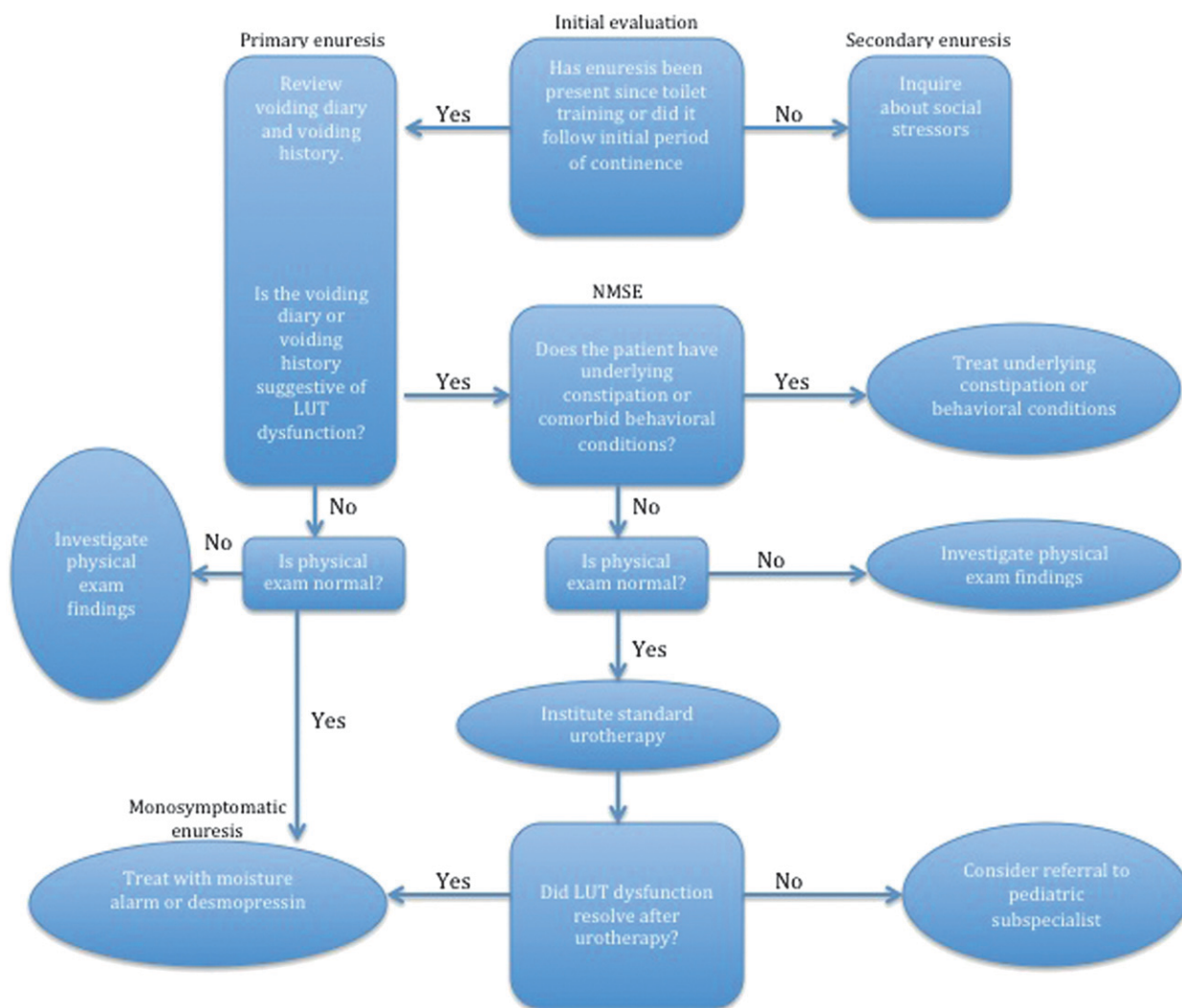


Figure 1. Algorithm for evaluation and management of children with enuresis.

physical therapists with expertise on pediatric pelvic floor dysfunction.

OTHER ADVANCED TECHNIQUES

α -Blockers

For children with evidence of functional bladder outlet obstruction who do not improve with first-line therapy, α -adrenergic antagonists (α -blockers) are sometimes used to facilitate more coordinated bladder emptying. Initially designed for treating men with LUT dysfunction secondary to benign prostatic hypertrophy, these medications have also been used for treatment in pediatric LUT dysfunction. (10) Selective α -blockers improve bladder emptying by their targeted relaxing effect on the bladder neck and proximal urethra (internal sphincter under autonomic innervation) during micturition. The Food and Drug Administration has

not formally evaluated these medications for this indication, and use in children should not be undertaken without disclosure to the family about off-label use.

Botulinum Toxin

Botulinum toxin A is another promising pharmaceutical agent for management of refractory LUT dysfunction. This is investigational at this time and should only be used under the supervision of a pediatric urologist in a research setting.

ENURESIS-SPECIFIC TREATMENTS

Once constipation, behavioral comorbidities, and LUT dysfunction have been addressed, standard enuretic therapies can be instituted if enuresis is still present. Each of the below therapies has strong research evidence for recommended use in children converted from NMSE to MSE.

Behavioral Modification

Data from randomized trials on the efficacy of behavioral therapy are lacking, but clinical experience (ie, level IV evidence) would suggest that this approach is beneficial. All patients with enuresis receive education and strategies to optimize bladder behavior. Children should attempt to void regularly during the day and just before going to bed for a total of 6 to 7 times daily. High sugar- and caffeine-based drinks should be avoided, particularly in the evening hours. Daily fluid intake should be concentrated in the morning and early afternoon, and fluid and solute intake should be minimized during the evening. Parental waking of the child to void when the parents go to bed is generally unreliable because the children will wet the bed randomly throughout the sleep cycle. Similarly, results from bladder-stretching exercises are mixed and generally anecdotal.

Moisture Alarm

Commercially available moisture alarms, when used properly, are effective treatments for MSE. The moisture alarm aims to strengthen the relationship between the full bladder and the sleeping brain and represents classic conditioning therapy. The alarm will sound as soon as moisture is detected in the child's underwear; however, it is crucial that parents use the alarm as a tool to fully awaken the child and have the child void before returning to sleep. With repetition, the child will learn to suppress micturition or may awaken spontaneously with a full bladder, obviating the need for the alarm. With proper use, 50% of children will be dry and have a durable response after several weeks of alarm therapy. (7)

Desmopressin

Desmopressin is the first-line pharmaceutical option for enuresis. The medication is an analog of vasopressin (also known as antidiuretic hormone) and works at the level of the nephron to decrease overall urine production. It does not have any central effect and does not increase spontaneous arousal with the sensation of a full bladder. Approximately 30% of children will be dry with this treatment, and another 40% will partially respond. Identification of children with nocturnal polyuria will markedly improve the response rate by selecting ideal candidates for desmopressin. Nocturnal polyuria is determined by weighing overnight pads and measuring the first morning void and is defined as nocturnal urine production greater than 130% of age-expected bladder capacity. (1)(2) The medication is generally safe and well tolerated, and adverse effects are rare. It is up to the discretion of the family whether to institute daily treatment or symptomatic management under situations where

enuresis would be problematic or socially unacceptable, such as slumber parties, camp, or school trips. (7)

Imipramine and Centrally Acting Medications

Imipramine, a tricyclic antidepressant, was the first medication noted to improve enuresis. Multiple randomized studies have found its efficacy to be approximately 50%. It has some direct anticholinergic activity on the bladder and may increase storage capacity to a small degree, but its primary mechanism is its central activation on the brain. The postulated mechanism of imipramine is the selective inhibition of neurotransmitter reuptake, but the exact central action of imipramine is poorly understood. It is no longer recommended as primary therapy for MSE because of concerns of cardiac toxic effects and the interaction of tricyclic antidepressants with many commonly prescribed medications. Thus, therapy with imipramine should only be instituted as a second-line agent after failing management with desmopressin and alarm therapy. (7)(8)

Other centrally acting medications, specifically norepinephrine reuptake inhibitors, also have promise in treating enuresis; however, these should not be routinely prescribed outside a tertiary care setting.

Anticholinergics

Monotherapy with anticholinergic drugs, such as oxybutynin or tolterodine, has been found not to be effective as a first-line of treatment for MSE in a placebo-controlled trial. (14) Although evidence of efficacy from randomized trials is lacking, uncontrolled studies have revealed improvement in some children with NMSE, presumably because many of these children have a reduced functional bladder capacity or nocturnal detrusor overactivity. (15) The therapeutic role of anticholinergics is clearer in combination therapy in the treatment of children with MSE who are refractory to desmopressin monotherapy. In a double-blinded, randomized, placebo-controlled study, children with primary MSE in whom the maximal dose of desmopressin monotherapy has failed received either extended-release tolterodine or placebo with desmopressin. With a generalized estimating equation approach, there was a significant 66% reduction in the risk of a wet episode compared with the placebo group. (16)

Alternative Therapies. Other drugs, including indomethacin, ephedrine, atropine, furosemide, and diclofenac, have been tried in the treatment of enuresis. A recent systematic review of randomized trials of drugs other than tricyclic antidepressants and desmopressin found that although indomethacin, diclofenac, and diazepam were better than placebo in reducing the number of wet nights, none of the drugs was better than desmopressin. (17) A second review of

complementary approaches, such as hypnosis, psychotherapy, and acupuncture, found limited evidence from small trials with methodologic limitations to support the use of such modalities for the treatment of enuresis. (18)

Summary (Figure 1)

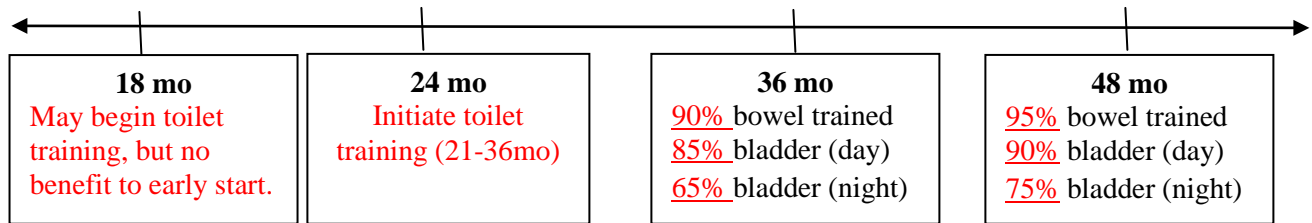
- On the basis of some research evidence and consensus, up to one-third of patients with enuresis will have daytime urinary symptoms indicative of lower urinary tract (LUT) dysfunction. (8) (9)
- On the basis of international consensus, children with enuresis and LUT dysfunction are correctly identified as having nonmonosymptomatic enuresis (NMSE) (formerly termed *diurnal enuresis*). (1)(2)
- On the basis of some research evidence and consensus, an adequate voiding and elimination history is the primary tool in differentiating between MSE and NMSE. (2)(7)(8)
- On the basis of some research evidence and consensus, therapy for NMSE is based on addressing underlying LUT dysfunction, constipation, and comorbid behavioral conditions before addressing enuresis. (2)(8)(9)(12)
- On the basis of some research evidence and consensus, treatment of underlying BBD and comorbid conditions will often result in improvement or resolution of enuresis. (2)(8)(9)(12)
- On the basis of international consensus, if enuresis is still present and a concern after treatment of underlying LUT, specific medical or behavioral therapy for enuresis should be offered to the family. (2)(8)

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Urinary Incontinence Quiz

1. **Flashback:** Complete the following **toilet-training timeline** (*%iles from BRS, 2005*):



2. What percent of 6 to 7-year-old children struggle with **bedwetting**? 15%

3. What percent of children with bedwetting also have **daytime wetting**? 33% or 1/3

4. MSE arises from physiologic disturbance of what three primary organs?

kidney -- nighttime concentrating defects (urine production >130% of EBC

EBC=30mL + age in yearsx30mL)

bladder -- small capacity (<50% EBC) or overactive

brain -- lack of arousal in response to stimulus to void

5. Of children with urinary incontinence 20-30% have comorbid behavioral conditions including ADHD, ODD, and conduct disorder.

6. Secondary enuresis occurs in children who have nocturnal incontinence after a dry period lasting at least six months and is often related to a recent severe stress.

7. If a child has one parents who had PMNE, the chance the child will have PMNE is nearly 50%

8. If a child has two parents who had MSE, the chance the child will have PMNE is 75%.

9. BBD stands for bladder-bowel dysfunction and is a combination of low urinary tract dysfunction and bowel dysfunction. LUT symptoms include frequency (>8 voids/day), decreased frequency (<or= 3 voids/day), dysuria, hesitancy, urgency, or intermittency. Bowel symptoms include constipation, encopresis, or fecal incontinence.

10. List three medications to treat PMNE. What is the mechanism of action? Side effects?

desmopressin	decreases urine production at nephron	hyponatremia
imipramine	anticholergic effect on bladder, CNS activation	cardiotoxicity
oxybutynin	increase bladder capacity, decr overactivity	constipation

Enuresis Cases

Case 1:

Luke is a 4.5 year old male who presents to the office with his mother with a chief complaint of bed-wetting. She reports that his 3 older sisters were all toilet trained by this age, and she is concerned by his delay.

Before taking your history, are you concerned?

Not immediately— dryness is expected to be achieved by **5 years of age**; if not, the child is diagnosed with E. Approximate bed-wetting rates are, as follows. (**Boys are 3x more likely to wet the bed than girls**):

- Age 5: 20%
- Age 6: 10–15%
- Age 7: 7%
- Age 10: 5%
- Age 15: 1–2%
- Age 18–64: 0.5–1%

What else do you want to know?

- **HPI:**
 - When was Luke potty-trained? When, if ever, was he dry during the day and/or during the night? (*helps distinguish primary vs. secondary nocturnal enuresis*)
 - What is the pattern of his enuresis? # nights/week; # episodes per night
 - What is his fluid intake, including caffeine, at nighttime?
 - How do his parents respond to his “bedwetting”? Any interventions so far?
- **ROS:** polyuria, polydipsia, urgency, frequency, dysuria, abnormal urine stream, constant wetness, bowel complaints (*15% of children with enuresis also have encopresis*)
- **PMHx:** UTI? Sleep Disordered Breathing? Neurologic disorders? Developmental delay? ADHD?
- **FamHx:** Were any of the parents or siblings bed-wetters?

Luke’s mother alerts you to the fact that she needs to leave in 10 minutes to pick her older children up from the bus stop. What rapid screen questions can help you distinguish between MSE and NMSE?

- previously dry for 6 months? indicates NMSE/ SNE
- daytime urinary symptoms? NMSE
- constipation or soiling? NMSE
- recent psychological stressor? SNE

***If the answer to all these questions is no, then likely straightforward PMNE.**

Luke's mother reports that he achieved daytime dryness around age 3. He has never been dry at night, however, and has always worn pull-ups to bed. He has a wet pull up most nights of the week, and mother is unsure of how many episodes per night. Luke has had no intermittent or constant daytime wetness, dysuria, polyuria, or urgency. Mother reports a soft daily bowel movement most days. Mother can not identify any recent psychological stressors including no additions to the family and no loss of family members due to death, deployment, or divorce, and no new school or childcare setting.

Luke's mother is now quite anxious to leave, but you let her know you would like to examine Luke before he goes. She agrees while dialing a friend to pick up her other children from the bus stop.

What parts of the exam are particularly important to evaluating Luke's enuresis?

- General hyperactivity defiance developmentally appropriate?
- GI: distended bladder? Fecal impaction?
- Urogenital: evaluation of the phallus and meatus for stenosis normal placement
- Neurologic: LE muscle tone and coordination, DTRs, sensation; sacral dimple/tuft

Luke's exam is as follows:

T 37, P 110, R 20, BP 107/64, Ht 102 cm (25th percentile), Wt 16.2 kg (25th percentile). He is alert and active, in no distress. HEENT and neck exams are negative. His lungs are clear bilaterally. His heart has a normal rate and rhythm, normal S1 and S2, and no murmurs. No masses, organomegaly, or tenderness are appreciated on abdominal exam. Bowel sounds are present. He has no inguinal hernias. He has a circumcised penis of normal size. The meatus is normally placed and sized and no phimosis is present. His testes are descended bilaterally and are of normal size (Tanner stage 1). His back is straight with no midline defects. His extremities and muscle tone are normal. His gait is normal. His speech and behavior are age-appropriate.

What is your diagnosis? How will you counsel mom?

Normal 4.5 year-old boy. (*See answer to 1st question*) Reassure mother that bladder control is often obtained by 5 years, but that 20% of children still wet the bed at this age—a percentage which decreases yearly. Point out that Luke's risk is increased due to his father's history.

Recommend that both parents are supportive of Luke's dry nights and avoid criticism of wet nights. Support their efforts to avoid fluid intake 2 hrs before bedtime and emptying his bladder at bedtime. There is probably no benefit to nighttime awakenings, bed-wetting alarms, or other behavioral interventions at this point, since this is still developmentally normal.

The next time you see Luke is 4 years later at your new post-residency duty-station in Guam, where his family has coincidentally PCS'd too! He is now 8.5 years-old and presents with his father, who reports that Luke is still wetting the bed, now 2-3 times per week, 1-2 times per night. As before, Luke will occasionally wake up wet in the middle of the night and change his own underpants and sheets; on other nights, his parents will find him wet in the morning. There is no diurnal enuresis. There have been no changes to PMHx, ROS, and PE from 4 years ago.

What is your diagnosis now? Do you want to do any further work-up?

PMNE = nocturnal wetting in a child who has never been dry on consecutive nights for longer than 6 months. Laboratory tests, other than a screening U/A, are not necessary for patients who have nocturnal enuresis. *The screening U/A will give you spec grav (to r/o DI), glucose (to r/o DM), and leukocyte esterase and nitrite (to r/o UTI).*

How will you counsel mom and patient? What are your treatment recommendations?

Counseling:

- Explain that the causes of PMNE are not understood, but there is likely a role of genetic factors, sleep factors, abnormal bladder dynamics, altered ADH release, psychological influences, and **maturational delay**.
- Reassure her that the rate of bed-wetting decreases as years pass, and he will likely outgrow the problem. Children 5-9 yrs have a **spontaneous cure rate of ~15% per year**. Adolescents 10-18 yrs have a spontaneous cure rate of 16% per year.

Treatment:

- Treatment includes behavioral and medical approaches. **The most effective long-term treatment of mono-symptomatic bedwetting is a bedwetting alarm** (success rates of 70% with good adherence, with resolution in 3-4 months). *See Tables below from “Evaluation and Management of Enuresis” (N Engl J Med 2009; 360: 1429-36.)*

Recommendations for the Use of Alarm Therapy.*
Use as first-line therapy — consider before prescribing medication
Continue therapy for at least 2 to 3 months
Have child wear alarm every night
Motivate child and parents to participate
Have both parents and child arise each time the alarm goes off — children quickly learn to turn off alarm and fall back to sleep
Have child go to bathroom and void each time alarm goes off
Inform family that first few weeks of therapy are the most difficult — arrange an early follow-up appointment to monitor progress and address any problems
Inform family that failure of child to wake or of parents to wake child are the most common reasons for failure of alarm therapy

Would you use DDAVP in this patient? What are your treatment considerations?

Desmopressin is **60-70% effective** (defined as a 50% reduction in wet nights); however, the **relapse rate is 80%**. The PIR article recommends that patients use the medication nightly for 3 months and then stop to see if the patient has outgrown the problem. Other providers will use DDAVP for “special occasions” only (e.g. sleepovers, summer camp, etc.).

The only serious adverse event reported with DDAVP is **symptomatic hyponatremia with water intoxication**—this is mostly reported with the nasal spray, which has a black-box warning. On evenings when DDAVP is taken, children should be instructed not to drink during the 1 to 2 hours preceding bedtime or for the rest of the night. DDAVP should be discontinued if HA, nausea, vomiting or other symptoms suggesting water intoxication develop.

What other co-morbid/contributing conditions may be present in this patient?

SDB, ADHD, developmental delay, difficult temperament, constipation/encopresis.

Case 2:

Holly is a 7 year-old female who presents with chief complaint of “ER F/U UTI”. You learn that Holly was seen in the ER a few days ago for ongoing urinary incontinence. ER clean-catch specimen U/A was positive for leukocyte esterase. She was diagnosed with a UTI and started on Bactrim but her parents are concerned and her symptoms have not improved.

What else do you want to know?

- Results of urine culture? Any prior evaluation for incontinence?
- Any other medical problems? Constipation? Neurologic dysfunction? Psychiatric issues?
- Toilet training history? Current toileting and hygiene practices?
- Family history of urinary incontinence?

Holly’s father takes her out of the room, while her mother tells you that Holly has struggled with daytime and nighttime wetting since they started potty-training at age 2. She has never had a dry period and usually wears pull-ups at night. Her PMHx is significant for ADHD, managed behaviorally. Mother denies a history of constipation. She has never had any imaging, and mother had normal prenatal ultrasounds. There is no family history of urinary incontinence.

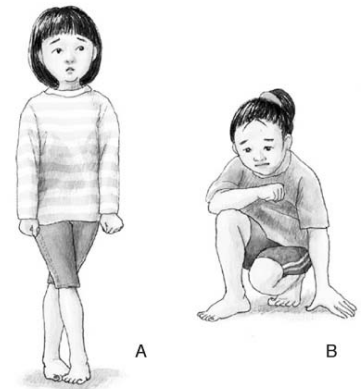
Before doing your exam, what is your working diagnosis? What other historical points can help you narrow your differential?

Holly has daytime incontinence so this is NMSE. Daytime wetting can be classified as a **storage problem** vs. an **emptying problem**. Children with storage problems may have hypersensitive bladders or inadequate sphincter tone, both of which lead to urinary leakage. Children with emptying problems may have “lazy” bladders or high sphincter tone, both of which lead to difficulty completely emptying the bladder. You can ask the following:

- Urgency (storage) vs. hesitancy (emptying)?
- Wet *before* voiding (storage) vs. wet *after* voiding (emptying) vs. *always* wet (anatomic)
- Urinary flow patterns (see chart)

Mother reports that it seems as if Holly “always has to go”. She has noticed that Holly will do the “pee pee dance,” squat on the floor, or sit at the hard edge of her chair prior to wetting herself. When mom notices these behaviors, she will try to pick Holly up and quickly move her to the bathroom, but this usually results in an accident which is typically small in volume, but still requires a change in underwear.

What is the sign demonstrated in Picture A? What is the most likely diagnosis? Vincent’s curtsy, urge incontinence



Given this likely diagnosis, what do you expect to find, if anything, on physical exam?

The PE for any type of daytime incontinence should focus on genitourinary abnormalities (female epispadias, labial adhesions, and intralabial masses); back and sacrum (asymmetric gluteal crease, sacral dimple, hairy patch); rectum (tone, fecal mass); abdomen (distension, masses—stool or enlarged bladder/kidneys). In this patient, for whom urge incontinence is suspected, her exam is likely to be **normal**, other than perhaps evidence of constipation.

Holly’s exam is completely normal, except for hard stool palpated in the LLQ and impacted stool on rectal examination.

Does this change your diagnosis? No. **Constipation supports NMSE**, particularly urge syndrome. It is possible that the pressure effect of stool in the descending or sigmoid colon can trigger an uninhibited detrusor contraction.

What further work-up, if any, will you recommend?

- Bladder U/S for post-void residual (PVR) and bladder wall thickness.
- Uroflowmetry
- Consider pediatric urology referral

What are your management recommendations? *See Table from (N Engl J Med 2009; 360: 1429-36.)*

Recommendations for the Use of Behavioral Therapy.*
Remove underpants and have child void in toilet at start of every day
Encourage child to avoid holding urine
Encourage voiding at least once every 2 hr, at least several times during school day, and often enough to avoid urgency and incontinence†
Facilitate easy access to school toilets with a note to the teacher
Have child drink a liberal amount of water during morning and early afternoon hours, a total of at least 30 ml per kilogram of body weight†
Minimize intake of fluids and solutes after dinner unless child is participating in evening sports or social activities†
Encourage a daily bowel movement, preferably after breakfast and before child leaves for school
Have child use optimal posture to relax pelvic-floor muscles, facilitating good emptying of bowel†‡
Encourage the child to eat foods that soften stool and to avoid foods that harden stool
Encourage the child to engage in physical activity and discourage prolonged sitting in front of television or computer†

- **Treat constipation:** *See Constipation Module*
- **Proper voiding methods:** Double-voiding, sitting backwards on toilet-seat; bladder training/pelvic floor training exercises to strengthen external sphincter/relax detrusor.
- **Biofeedback:** *See Extra Credit Reading*
- **Medication:** Can be helpful but is not typically first-line therapy. Consider anticholinergic (e.g. Oxybutynin = Ditropan) for storage problem.

Enuresis Board Review

1. A 4-year-old girl presents with a 10-day history of increased urinary frequency but no associated dysuria or fever. She often voids a few times per hour during the day, but does not awaken at night to void. She typically sleeps 9 hours per night and is dry on awakening each morning. She was toilet trained at 2½ years of age. Her parents report that her older brother recently started school, and she has seemed a bit restless in recent weeks. Findings on her physical examination are unremarkable. A urinalysis shows a specific gravity of 1.020; pH of 6.0; and negative findings for blood, protein, leukocyte esterase, and nitrite. Urine culture results are negative.

Of the following, the MOST appropriate next step in treating this patient is to

- A. order voiding cystourethrography
- B. place the child on a timed voiding program
- C. prescribe a 10-day course of antibiotics
- D. reassure the parents that the problem should be short-lived**
- E. start the child on a laxative to treat any component of constipation

The child described in the vignette has the clinical picture of **pollakiuria**. This condition of extraordinary urinary frequency typically occurs suddenly in toilet-trained children, causing them to need to void small urine volumes every 5 to 20 minutes without associated dysuria, abdominal pain, or fever. Affected children are typically 4 to 6 years old. Another characteristic feature is marked symptoms during the day that usually resolve completely during sleep and the lack of nocturnal enuresis. The urinary tract is structurally normal, and, therefore, imaging such as ultrasonography and voiding cysto-urethrography generally is not needed. Because urine cultures are negative, there is no role for antibiotic treatment. Pollakiuria may be triggered by psychosocial stress such as a death in the family or parental divorce. The prognosis is excellent, with anticipated resolution of symptoms within 2 to 6 months.

A more significant type of voiding dysfunction that should be considered in a child who has urinary frequency is due to an **unstable (overactive) bladder**. Affected children often experience urgency due to uninhibited bladder contractions and frequently have daytime and nighttime enuresis. The presence of nocturnal enuresis distinguishes the child who has an unstable bladder from one who has pollakiuria. Children who have unstable bladders compensate for their uninhibited bladder contractions by learning to contract the external urinary sphincter voluntarily to avoid incontinence, often assuming postures such as squatting, leg crossing, or Vincent curtsy (using the heel to provide pressure at the perineal region). Because this condition is not short-lived and may be associated with urinary tract infections from urinary retention, its prognosis is not as favorable as that of pollakiuria. Therefore, timed voiding is recommended. For those unable to void often enough, anticholinergic agents are recommended.

Treatment of **constipation** is useful in children who have dysfunctional elimination or recurrent urinary tract infections, but it does not appear to have a role in children who have pollakiuria or bladder instability (overactive).

2. A 6-year-old girl presents with complaints of persistent daytime and nighttime wetting. She has no dysuria, frequency, urgency, polyuria, polydipsia, abdominal pain, or constipation. According to her mother, the girl has shown signs of toilet training since 3 years of age, using the bathroom whenever she felt the urge to urinate. Despite these behaviors, however, her mother states that her daughter is "always wet." The child is doing well in school and has no physical limitations. She has had no urinary tract infections. Findings on her physical examination are normal. Urinalysis reveals a urine specific gravity of 1.025; pH of 6; and negative blood, protein, leukocyte esterase, nitrite, and microscopy findings. A urine culture is negative.

Of the following, the MOST likely explanation for this child's clinical condition is

- A. ectopic ureter**
- B. neurogenic bladder
- C. pollakiuria
- D. ureterocele
- E. viral cystitis

The history described for the child in the vignette strongly suggests the diagnosis of **ectopic ureter**. The normal ureteral insertion site is into the bladder trigone. When insertion occurs caudal to this site, it is defined as ectopic. Ectopic ureters can occur in both males and females, but they are six times more common in females. The true incidence is unknown, but autopsy studies have demonstrated their presence in 1 in 1,900. Ectopic ureters often occur in association with a duplicated collecting system. Typically, the ectopic ureter transports urine formed from the upper pole of a duplex collecting system. The renal unit associated with the ectopic ureter generally is small and dysplastic, making it somewhat difficult to detect with routine U/S. Ectopic ureters are B/L in 10% of cases.

The sites of ectopic ureters in females include the bladder neck, urethra, and vagina; in males, the locations include the posterior urethra (50%), seminal vesicle, and bladder neck. Because the orifice for insertion of ectopic ureters in males is located proximal to the external bladder sphincter, males do not present with incontinence.

Diagnosing ectopic ureter can be difficult and frequently delayed when the child is misdiagnosed as having **voiding dysfunction**. A history of constant wetness in an otherwise healthy female who is toilet trained should alert the clinician to this diagnosis. The diagnostic evaluation can be challenging. In one study, ultrasonography was diagnostic in only 2 of 12 cases. Furthermore, the ultrasonographic finding in most children ultimately diagnosed with ectopic ureters is either a duplex collecting system (on one or both sides) or normal. A normal ultrasonography result could falsely reassure the clinician and family. Ultrasonography is noninvasive and helpful in identifying individuals "at risk" for an ectopic ureter by demonstrating a duplex collecting system. However, the clinician should pursue further diagnostic studies aggressively when ectopic ureter is suspected.

Until recently, the diagnostic study of choice was excretory urography. The current recommendations by most radiologists and urologists is magnetic resonance urography (MRU) to demonstrate the small, dysplastic renal unit and its associated ectopic ureter and the location of its ureteral orifice. Imaging with MRU avoids the ionizing radiation associated with excretory urography or computed tomography scan. Voiding cystourethrography has no role in the diagnostic evaluation of this disorder.

Neurogenic bladder usually is associated with overflow incontinence and recurrent urinary tract infections and typically is seen in children who have spina bifida, spinal cord injury, or tethered cord. **Pollakiuria** is a condition of extraordinary urinary frequency that occurs after toilet training, is short-lived (weeks to months), and frequently is associated with psychosocial stress. A **ureterocele**, like ectopic ureter, often is seen with a duplex collecting system, but the typical presentation is urinary tract infections in the first postnatal year due to urinary stasis. **Viral cystitis** is a short-lived condition that is associated with symptoms of dysuria, frequency, and urgency and findings of pyuria on urinalysis but negative bacterial cultures.

3. You are seeing a 7-year-old boy for occasional nocturnal enuresis. His weight and height are at the 50th percentile for age, his blood pressure is 110/66 mm Hg, and there are no unusual findings on physical examination. Urinalysis shows a specific gravity of 1.030, pH of 6.5, 2+ blood, and no protein. Urine microscopy reveals 10 to 20 red blood cells/high-power field and no casts or crystals. Results of a repeat urine sample 3 weeks later are unchanged. Laboratory findings include:

- Blood urea nitrogen, 12.0 mg/dL (4.3 mmol/L)
- Creatinine, 0.4 mg/dL (35.4 μmol/L)
- Complement component 3 (C3), 110.0 mg/dL (normal, 86.0 to 166.0 mg/dL)
- Complement component 4 (C4), 22.0 mg/dL (normal, 13.0 to 32.0 mg/dL)
- Antinuclear antibody, negative
- Erythrocyte sedimentation rate, 6 mm/hr

Of the following, the MOST appropriate next step is

- A. abdominal computed tomography scan
- B. referral for cystoscopy
- C. referral for renal biopsy

D. renal/bladder ultrasonography

- E. repeat urinalysis in 1 month

Microscopic hematuria is defined as a positive dipstick test for blood and more than 5 red blood cells/high-power field on microscopy. Persistent microscopic hematuria is defined as blood on urinalysis detected on repeat samples over a 1-month period. Children who have persistent microscopic hematuria, such as the boy described in the vignette, require investigation for an underlying cause. The urgency of such an evaluation in the absence of symptoms is predicated on whether the patient has accompanying proteinuria (>1+ on a dipstick). Those who have proteinuria require urgent evaluation to look for an underlying glomerulopathy in which disruption of the glomerular capillary barrier (as occurs in glomerulonephritis) results in RBCs and albumin gaining access to the urinary space.

Up to 4% of all children may have microscopic hematuria on a routine screening urinalysis. Based on this high incidence, the initial recommendation for a child who has isolated, asymptomatic microscopic hematuria is to undergo repeat urinalysis in 2 to 3 weeks time. If the hematuria persists, as occurred in the patient in the vignette, the clinician should evaluate the patient for an underlying genitourinary problem. This evaluation typically includes renal function tests (serum creatinine) and serologic testing for an underlying immune complex-mediated glomerulonephritis (complement components 3 and 4, antinuclear antibody). In addition, **renal imaging (renal/bladder ultra-sonography) to screen for cysts, stones, and tumors is indicated.**

Abdominal computed tomography scan is not indicated prior to a renal/bladder ultrasonography in this clinical setting. More invasive testing, such as cystoscopy, should not be undertaken unless there is a strong suspicion of bladder pathology, especially prior to screening with ultrasonography. Similarly, renal biopsy is not indicated in the absence of proteinuria, hypertension, azotemia, or gross hematuria. Repeat urinalysis is redundant because persistent hematuria already has been substantiated.

4. The mother of a 6-year-old girl reports during a health supervision visit that her daughter has nighttime wetting and occasional daytime accidents with urgency. She has no history of constipation, and no one else in the family has suffered enuresis. Her urinalysis reveals:

- Specific gravity, 1.020 ; pH, 7
- 2+ blood ; Trace protein
- Positive for nitrites; 3+ leukocyte esterase
- 5 to 10 red blood cells/high-power field (hpf)
- 20 to 50 white blood cells/hpf

Of the following, the BEST next diagnostic test to perform for this patient is

- A. Cystoscopy
- B. DMSA (technetium dimercaptosuccinic acid) renal scan
- C. Magnetic resonance imaging of the lumbosacral spine
- D. Renal/bladder ultrasonography**
- E. Spiral computed tomography scan of the abdomen

The child described in the vignette exhibits **nonmonosymptomatic enuresis, which is defined as nocturnal incontinence plus daytime voiding symptoms**. As is recommended for all patients who have enuresis, she underwent a urinalysis, which revealed marked pyuria with mild hematuria and possible bacteruria (nitrite-positive). These findings are strongly suggestive of a urinary tract infection (UTI). Further evaluation, in addition to a confirmatory urine culture, should include renal/bladder ultrasonography. This study can help screen for hydronephrosis and renal stones, which could increase the risk for a UTI.

Cystoscopy has a limited role in pediatrics for enuresis or hematuria; it is most useful to evaluate urinary obstruction and occasionally in the evaluation of gross hematuria without an underlying cause. DMSA scan is most useful as a follow-up study to evaluate for renal scarring in a child who has a history of pyelonephritis. Magnetic resonance imaging of the lumbosacral spine is a useful diagnostic test to evaluate for a possible tethered cord in a child who has an acquired neurogenic bladder. This is usually a second-line study after initial ultrasonography to screen for hydronephrosis. Spiral computed tomography (CT) scan of the abdomen is indicated for a child in whom a renal stone is suspected but who has negative findings on ultrasonography. The risks of radiation exposure with a CT scan always should be considered by the clinician, who needs to weigh the risks and the benefits of performing the study.

The search for an underlying organic cause of enuresis should be considered for all patients, but it is suggested by the history. Pertinent portions of the patient history include dysuria, frequency, and urgency (UTI); polyuria, nocturia, polydipsia, and nighttime thirst (**diabetes mellitus and urinary concentrating defects such as diabetes insipidus and renal dysplasia**); constipation (**dysfunctional voiding**); nighttime snoring (**sleep apnea** due to adenotonsillar hypertrophy); and new-onset constipation or gait disturbances (**tethered cord**). On physical examination, the clinician should examine the oropharynx for tonsillar enlargement, the abdomen for palpable stool, and the spine for sacral dimples or hair tufts (**spina bifida occulta**) as well as check the deep tendon and plantar reflexes. The urinalysis is an inexpensive and simple test to determine urine concentrating ability. Further evaluations, such as renal/bladder ultrasonography, are undertaken as clinically indicated.

Treatment of the underlying organic cause often results in marked improvement. Once a UTI is treated, the urinary symptoms and enuresis should resolve. **In a recent study, the incidence of enuresis was 42% in children who had obstructive airway disease**. In these patients, who had adenotonsillar hypertrophy and nocturnal enuresis, adenotonsillectomy resulted in improvement in 64% and complete resolution of enuresis in 33%. This patient cohort also showed improvement in daytime frequency and incontinence with adenotonsillectomy.