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.

- Describe diagnostic criteria, including differentiation of primary vs. secondary, and diurnal vs. nocturnal.
- Identify conditions in the differential diagnosis of, as well as risk factors for, nocturnal enuresis
- Perform assessment appropriate to the primary care setting, including input from home and school.
- Describe indications for referral to other professionals for evaluation or treatment of enuresis.

Pre-Meeting Preparation:

Please read the following enclosures:

- "Enuresis" (Peds in Review, 2009)
- Summary Tables for Nocturnal Enuresis & Daytime Incontinence
  - *From UpToDate, 2012 and AAFP, 2008*
- **"Show & Tell":** Be prepared to discuss a "home remedy" for nocturnal enuresis (e.g. bedwetting alarms, watches, etc.). Research online.

Conference Agenda:

- *Review* Enuresis Quiz
- Complete Enuresis Cases
- **"Show & Tell":** Discuss "home remedies" for nocturnal enuresis. *Faculty*—you may refer residents to The Bedwetting Store for examples.

Post-Conference: *Board Review Q&A*

Extra-Credit:

- International Children's Continence Society (ICCS) Terminology Report *(2006)*
- 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*

Enuresis

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Author Disclosure
Ms Graham and Dr Levy 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.

Objectives

After completing this article, readers should be able to:

1. Describe the causes of daytime wetting.
2. Discuss the pathophysiology and causes of nocturnal enuresis.
3. Understand the behavioral treatment of incontinence.
4. Characterize the medical treatment of daytime incontinence.
5. Know the treatments for nocturnal enuresis.

Introduction

Both day and night wetting can pose a significant problem for children, parents, and medical practitioners. The prevalence of day wetting in 7-year-old children is between 2% and 3% for boys and 3% and 4% for girls. Most cases represent a functional type of incontinence, with only a few cases due to an anatomic, neurologic, or psychiatric cause. Most children typically are trained prior to starting school, but those who continued wetting rated this happening as a significant embarrassment and life stressor. Wetting often is a significant complaint raised during a visit with the pediatrician. Data suggest that children who have prolonged enuresis have lower self-esteem.

Primary nocturnal enuresis (PNE) is defined as nocturnal wetting in a child who has never been dry on consecutive nights for longer than 6 months. It is estimated that between 5 and 7 million children and adolescents may suffer from this disorder. The incidence of PNE is based on age. Dryness is expected to be achieved by 5 years of age; if not, the child is diagnosed as having PNE. An estimated 10% to 15% of 7-year-old children still struggle with bedwetting. Nocturnal enuresis resolves at a rate of 15% per year, so 99% of children are dry by age 15 years. The social consequences of nocturnal enuresis lead many to seek medical attention.

To clarify day and night wetting, the International Children's Continence Society recently published new standardization for the terminology of enuresis. (1) They define incontinence as uncontrollable leakage of urine that may be intermittent or continuous and occurs after continence should have been achieved. Continuous incontinence means constant urine leakage, as in a child who has an ectopic ureter or iatrogenic damage to the external sphincter. Intermittent incontinence is urine leaking in discrete amounts either during the day, night, or both. Any wetting that occurs in discrete amounts at night is termed enuresis regardless of whether it is associated with daytime symptoms. Leakage that occurs during the day is daytime incontinence (no longer called diurnal enuresis). Dysfunctional voiding is defined by inappropriate muscle contraction during voiding and usually is associated with constipation and is referred to as dysfunctional elimination syndrome.

Abbreviations

ADH:	antidiuretic hormone
ADHD:	attention-deficit/hyperactivity disorder
DSD:	detrusor sphincter dyssynergia
PNE:	primary nocturnal enuresis
PVR:	postvoid residual
UA:	urinalysis
UTI:	urinary tract infection
VCUG:	voiding cystourethrography
VUR:	vesicoureteral reflux

Causes of Nocturnal Enuresis

The causes of nocturnal enuresis are not understood completely. Several theories have been proposed, including the role of genetic factors, alterations in vasopressin secretion,

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sleep factors, and abnormal bladder dynamics. Other mechanisms may include psychological influences, organic disease, and maturational delay.

Many parents of children who have enuresis report that their children sleep more deeply and are more difficult to arouse than other children. Early studies supported this controversial hypothesis, but numerous recent studies refute it. Controlled studies have shown no difference between children who do and do not have enuresis. No data support the concept that children who have enuresis wet during "deep" sleep, and wetting has been shown to occur throughout different sleep patterns. An association has been shown between obstructive sleep apnea syndrome and enuresis. Affected patients have increased atrial natriuretic factor, which inhibits the renin-angiotensin-aldosterone pathway, leading to increased diuresis. Tonsillectomy, adenoidectomy, or both have been shown to cure enuresis to a significant extent in this select group.

Based on circadian rhythms, nocturnal urine production is approximately 50% less than daytime urine production. As early as the 1950s, children who suffered enuresis were shown to have significantly increased nocturnal urine production compared with unaffected children. Nocturnal polyuria due to alterations in vasopressin release has been shown to be a factor in nocturnal enuresis. This theory is based on studies showing that children who have nocturnal enuresis have abnormal circadian release of antidiuretic hormone (ADH).

Bladder dysfunction, as evidenced by diminished bladder capacity and abnormal urodynamics, may play a role in nocturnal enuresis. Patients who have PNE have been shown to have smaller-than-normal functional bladder capacities at night, and urodynamic studies have demonstrated higher bladder instability at night compared with during the day. As expected, patients who have both daytime incontinence and nocturnal enuresis have a higher degree of functional bladder abnormalities and a higher failure rate with conventional treatment than patients experiencing nocturnal enuresis alone.

Evidence is strong that genetics plays a role in nocturnal enuresis. Studies have shown that when one parent had enuresis as a child, his or her child had a 44% chance of also experiencing the condition. If both parents were affected, this chance increased to 77%. Interestingly, the parental age of resolution often predicts when the child's enuresis should resolve. Studies of twins support the genetic role, with 68% concordance in monozygotic twins and 36% in dizygotic twins.

Psychological factors contribute to PNE. Some studies have shown a higher prevalence of enuresis in children who have attention-deficit/hyperactivity disorder (ADHD) compared with a control population. Surveys show that children who have ADHD have a 30% greater chance of enuretic events. Recent studies reveal that the reason may not, as previously believed, be inattention but may be a neurochemical effect.

Maturational delay as a hypothesis for enuresis may be the most unifying of the theories. In a large population study, children who had enuresis had more fine and gross motor clumsiness, perceptual dysfunction, and speech defects than did controls. Patients who had nocturnal enuresis differed less from controls compared with those who had both nocturnal enuresis and daytime incontinence. (2)

Secondary enuresis is defined as new-onset nighttime wetting on consecutive nights after a 6-month or greater period of dryness. Although very disturbing, usually this occurrence is not related to an organic cause. In some cases, a stressful event, such as the birth of a sibling, a move, or the death of a parent or grandparent, is the source. Secondary enuresis should be evaluated and treated like PNE; there is no need for additional laboratory work or imaging studies.

Evaluation of Nocturnal Enuresis

Evaluation of nocturnal enuresis starts with a history. It is important to determine whether the enuresis is primary or secondary. The pattern of enuresis also must be determined, delineating the number of nights per week and the number of episodes per night. The pattern of nighttime fluid intake should be documented, as should caffeine intake. The evaluation should include questions regarding polyuria, polydipsia, urgency, frequency, dysuria, abnormal urine stream, history of urinary tract infection, constant wetness, and bowel complaints (15% of children who have enuresis also have encopresis). A history of sleep disorders such as sleep apnea or insomnia and a neurologic and developmental history should be obtained. Family history is helpful and should be sought.

Most children who have PNE have normal findings on physical examination. Clinicians should focus on the gastrointestinal (GI), urogenital, and neurologic systems. If abnormalities are found, the child most likely does not have an isolated case of nocturnal enuresis. During the abdominal examination, the physician should look for a distended bladder or fecal impaction. The male urologic examination should include evaluation of the phallus and meatus; the female examination should focus on the introitus, looking for labial adhesions or urethral abnormalities. The neurologic examination should assess

lower extremity muscle tone and coordination, along with deep tendon reflexes and sensation. The skin over the spine should be inspected, looking for a tuft of hair, vascular marking, or a sacral dimple that might signify occult spinal dysraphism.

Laboratory tests, other than a screening urinalysis (UA), are not necessary in evaluating patients who have nocturnal enuresis. Urine specific gravity is measured to evaluate for diabetes insipidus. Glucose spillage may suggest diabetes mellitus, and the presence of bacteria may signify an infection. Urine culture should be obtained if the UA appears to show infection. Patients who have nocturnal enuresis and associated daytime incontinence, with or without encopresis, may warrant additional studies.

Urinary tract infection (UTI) in children who suffer enuresis should lead the clinician to consider imaging studies under certain circumstances, specifically renal and bladder ultrasonography and voiding cystourethrography (VCUG). Both studies should be performed in any boy who has a UTI, in girls who have a febrile UTI, in girls who are not toilet-trained who have a UTI without fever, and in girls who are toilet-trained and have recurrent afebrile UTIs (three or more in 6 months). Toilet-trained girls who have afebrile UTIs should undergo ultrasonography. If abnormalities are found, VCUG is indicated. Some clinicians extend the indications for imaging further. Blood testing rarely is needed unless there is associated renal disease or suggestive physical findings.

Treatment of Nocturnal Enuresis

Treatment of nocturnal enuresis includes both behavioral and medical options. Among the behavioral modifications are limiting nighttime fluid intake 2 hours before bedtime, limiting dairy products 4 hours before bedtime (to decrease urine output from osmotic diuresis), and voiding prior to going to sleep. Medical therapy includes desmopressin acetate, anticholinergic agents, imipramine, or combination therapy. Alarm therapy falls into both categories of treatment. Acupuncture and hypnosis are other treatments, but few data support their use.

Alarm Therapy

The bedwetting alarm is by far the most effective strategy for curing nocturnal enuresis, having reported success rates as high as 66% to 70%. Alarm therapy, however, is the most difficult method to employ. Its mechanism is unknown, but it is believed to be a conditioned response. The alarm must be used every night for success and may require 3 to 4 months for results. The family needs to be counseled prior to starting treatment and motivated for success to occur. The patient is instructed to wear underwear rather than paper underpants. Usually the patient awakens to the sound of the alarm (triggered by dampness in the device), but if the child does not wake, the parent must awaken and accompany him or her to the bathroom. Many children awaken more than once a night, which can be stressful on the family.

Advantages of alarm therapy are that it offers a real cure, with no recidivism and no adverse effects. Disadvantages include significant parental involvement because the alarm may not wake the child at first, with disruption of sleep for all family members. Alarm therapy works better in older children who are motivated to be dry. A patient is considered cured if he or she has worn the alarm for 1 month and it is not triggered because he or she remains dry.

Pharmacologic Treatment

Medications often are used in the treatment of nocturnal enuresis to help treat, rather than cure, the problem while awaiting natural resolution. The first-line choice is desmopressin acetate. Desmopressin is a synthetic analog of ADH. It works at the level of the kidney, reducing urine output overnight. Such reduction in urine volume overnight may not make the child completely dry, especially if the child has bladder instability and reduced functional bladder capacity at night. The response rate, as defined by a 50% reduction in wet nights, is 60% to 70%. Success rates generally are better in patients who do not have daytime incontinence and who have normal functional bladder capacities.

Desmopressin tablets are well tolerated and have very few reported adverse effects. However, reports of severe hyponatremia associated with seizures and deaths in children who have used the *intranasal* formulations of desmopressin have caused the United States Food and Drug Administration to advise clinicians not to use desmopressin in that form for treating PNE. (3) Also, desmopressin therapy should be suspended when children experience acute conditions that can cause fluid or electrolyte imbalance, such as fever, recurrent vomiting and diarrhea, or vigorous exercise.

Desmopressin has a dose-dependent reaction. The initial dose is one tablet (0.2 mg) taken 30 minutes prior to bedtime on an empty stomach because the polypeptide is absorbed rapidly in the stomach (if patients cannot swallow the tablet, it can be crushed and put in applesauce). The dose may be titrated to a maximum of 0.6 mg to achieve dryness. Desmopressin is maximally

effective in 1 hour and is cleared within 9 hours after administration. Therefore, the drug only works on the night it is consumed. We recommend that patients use the medication nightly for 6 months and then stop for 2 weeks to see if the patient has outgrown the problem. Practitioners and patients alike find that desmopressin either "works or it doesn't." Because the drug controls only one factor, nocturnal urine output, not all patients respond to this treatment alone. Relapse after short-term treatment is common.

Anticholinergic agents long have been used in the treatment of nocturnal enuresis. These drugs are especially effective for patients who have associated daytime wetting and urgency or frequency. They rarely are effective when used alone, but work well in combination with desmopressin. This combination often is a good option when the patient has nocturnal enuresis with reduced functional bladder capacity (with or without daytime incontinence) and has failed desmopressin therapy alone. Approved medications for use in children include oxybutynin chloride (approved in children 5 years or older in the short-acting form and in children 6 years and older in the once-a-day form). Another available anticholinergic that is not yet approved in children is tolterodine tartrate (2 to 4 mg). We have used this medication safely in our clinic, with parental consent, and have had good results.

Imipramine is a tricyclic antidepressant developed in the 1960s that continues to be used in the treatment of enuresis. Its action is unknown, but it appears to have both a weak anticholinergic effect as well as an antispasmodic effect on the detrusor muscle. Recently, imipramine has been found to increase concentrations of ADH release. It has been postulated that imipramine affects the arousal center of the brain by increasing arousal and suppressing rapid eye movement sleep. Wide variation in cure rates have been reported (64% to 80%), but when imipramine therapy is discontinued, especially abruptly, only 25% of patients remain dry long-term. Adverse effects are uncommon but include gastrointestinal disturbance, sleep disturbances, anxiety, and dry mouth. Most serious adverse effects are associated with overdose and include fatal cardiac arrhythmias, seizure, hypotension, and coma. Parents should be notified of these risks, which can be a threat to younger siblings as well as to patients.

Daytime Wetting

Daytime wetting, whether dribbling or soaking, can have a significant psychological impact. When asked to rank stressful life events, one group of investigators found that children rated wetting their pants at school third out of 20 stressful events. Another study revealed that parents reported more psychological problems in their children older than 7.5 years of age who had daytime wetting compared with children of the same age who had no daytime wetting. In addition, children who have ADHD are disproportionally affected by day and nighttime wetting. One study showed a 30% incidence of enuresis in children who had ADHD compared with 5% of children who had no ADHD. Also, children experiencing stressful events such as divorce, death of family members, or abuse during the ages of 2 to 5 years . . . have a higher incidence of daytime wetting.

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Understanding and sorting through the causes of daytime incontinence requires an understanding of the normal micturition cycle, which involves two distinct processes: bladder filling/storage and bladder emptying. Filling and storage of the bladder are under control of the sympathetic nervous system, which allows the bladder to fill at low pressure while outlet resistance increases. The sympathetic system mediates inhibition of detrusor activity while its neurotransmitter norepinephrine increases activity of the bladder neck and proximal urethra. Bladder emptying occurs as a result of bladder contraction mediated through acetylcholine from parasympathetic innervation. At the same time, coordinated voiding requires inhibition of sympathetic outflow to the bladder that results in relaxation of the trigone and proximal urethra and impulses from the pudendal nerve that act to relax smooth and skeletal muscle of the bladder neck, thereby lowering outlet resistance. Thus, coordinated voiding involves an intact nervous system,

muscle development, brain development, and an anatomically normal urinary tract.

Daytime wetting has many causes. Most cases result from alterations in function, but it is important to seek specific disorders.

Classification of Daytime Wetting

Most daytime wetting can be classified either as a storage or an emptying problem. For some patients, however, a combination of the two mechanisms leads to incontinence. The evaluation, management, and treatment of daytime incontinence are straightforward after determining which of the two problems is occurring.

Children who have storage problems can be subdivided into neurologically normal children who cannot fill and store urine at low pressure; neurologically abnormal children who have high pressure (noncompliant) bladders with leakage; children whose bladders are hypersensitive, which results in leakage; and children who have inadequate sphincter tone, with or without an identifiable cause.

In contrast, emptying problems are identified by a failure to empty the bladder completely, on command, at low pressure, and with no significant residual urine. The mechanism may be neurologic, anatomic, muscular, or functional (ie, inability by a neurologically normal child to relax the sphincter during voiding).

Evaluation of Daytime Wetting

The history is the most valuable tool in the evaluation of daytime wetting and must include a detailed voiding history. Necessary information includes: age of toilet training, pattern of wetting, volume of wetness (dribbling versus soaking), number of times per day the child is wet, whether the child has ever been dry, what time of day (eg, during play) incontinence occurs, any history of UTIs, number of voids per day, any associated nighttime wetting, and prior evaluation and treatment.

A detailed history of bowel function is important. Among the relevant information is number of stools per week, consistency of stools, presence of frank encopresis or "skid marks" (often misinterpreted as improper wiping), and presence or absence of abdominal pain. A good social history should focus on the presence of abuse, parental attitude toward wetting, and any psychological stressors that may be present.

The physical examination should include close attention to genitourinary abnormalities, back or sacral anomalies, and the rectum. Genitourinary abnormalities that raise suspicion include meatal stenosis, hypospadias, tight phimosis, female epispadias, labial adhesions, and intralabial masses, which could represent a ureterocele or an ectopic ureter. The back and sacrum should be examined for an asymmetric gluteal crease, sacral dimple, vascular malformation, or hairy patch over the sacrum, which might indicate underlying spinal cord malformation. The rectum should be assessed for both tone and the presence of a large amount of fecal material. Abdominal examination should assess for distension, masses, and stool in the sigmoid. The perineal skin should be evaluated for maceration, indicating significant incontinence.

Laboratory evaluation of patients who have daytime wetting begins with a UA and urine culture. Bladder ultrasonography to assess for a postvoid residual (PVR) is imperative. Bladder wall thickness should be measured to evaluate the possibility of bladder trabeculation, signifying overcontraction of the detrusor muscle. Imaging studies should be performed for children who have UTIs, using the guidelines outlined previously. In addition, any child who has both daytime wetting and a UTI should undergo ultrasonography.

A unique procedure that assesses the patient's urinary stream both quantitatively and qualitatively is the uroflow test. The patient voids into a machine equipped with electric sensors that continuously record the rate of flow. A printout is generated that provides information on flow rate and quantity, and a graphic curve is created that can aid in diagnosis. Typical patterns are seen in such conditions as urge incontinence, emptying problems such as detrusor sphincter dyssynergia (DSD), or a true obstruction such as posterior urethral valves or urethral stricture in males. Uroflow testing is recommended for children who have daytime wetting.

Ectopic ureter should be considered for female patients who have no history of day- or nighttime dryness and characteristic "constant dribbling." This possibility should be evaluated by magnetic resonance urography, contrast computed tomography scan, or intravenous pyelography. Patients found to have an ectopic ureter should be referred to a pediatric urologist because it is a potential surgical problem.

Urodynamics are performed to evaluate children who do not respond to traditional therapy or patients in whom a tethered spinal cord is suspected. This condition should be suspected especially in patients who have daytime incontinence, nocturnal enuresis, and encopresis. Some patients, however, have tethered cord syndrome that initially presents with no bowel involvement. If tethered cord syndrome is a concern, based either on abnormal urodynamics or a suspicious physical finding, magnetic resonance imaging of the lumbosacral cord is mandatory.

Manifestations of Storage Problems

Clinical manifestations of storage problems are categorized as urge incontinence, overflow incontinence, diurnal enuresis, and urinary frequency (with or without actual wetness).

Urge incontinence, sometimes referred to as urge syndrome, is characterized by frequent attacks of a strong desire to urinate countered by holding maneuvers such as squatting, dancing, and curtseying. This condition is caused by uninhibited bladder contractions and reflexive sphincter contraction to minimize wetting. Often, the amounts of urine lost are small and cause dampness rather than soaking. Children who have urge syndrome may experience suprapubic and low back pain as well as referred pain to the genitalia. Functional bladder capacity generally, but not always, is small for age. Urge incontinence also can be associated with nighttime wetting.

The pattern of daytime wetting that is referred to as overflow incontinence is caused by infrequent and incomplete voiding. This condition develops over time. The bladder becomes large, and the urge to urinate is inhibited easily. Over time, affected children lose their awareness of bladder filling and, therefore, have significantly decreased sensation that they need to void. The amount of wetness varies but usually is large.

Daytime incontinence is described by normal but infrequent or delayed voiding, especially associated with distraction or play. The amount of urine lost varies from small to large. Such characteristics describe children who present with no idea that they are going to wet until leakage occurs. The association of behavior problems in this subgroup is high. Sudden development of daytime incontinence after continence has been achieved should prompt a referral to a pediatric urologist.

Urinary frequency, generally referred to as benign urinary frequency of childhood or pollakiuria, is a very common complaint that is characterized by a sudden need to urinate very frequently, sometimes up to 30 times per day. There is rare nocturia, no dysuria, and no actual urine leakage. Affected patients do not require an extensive radiologic evaluation. Pollakiuria occurs in younger children, usually in those 3 to 8 years of age, and usually is self-limited. Interestingly, affected children often do not respond to anticholinergic therapy. The cause is believed to be related to psychological stressors.

Manifestations of Emptying Problems

Clinical manifestations of emptying problems often, but not always, are more severe in degree than are storage problems. Emptying conditions are categorized, from the least to the most severe, as lazy bladder syndrome, DSD, and nonneurogenic neurogenic bladder (Hinman syndrome).

Lazy bladder syndrome describes a voiding disorder in which children void three or fewer times a day. The bladder becomes enlarged, and the detrusor muscle begins to decompensate. Patients must strain their abdominal muscles to void. They have a poor and often intermittent stream that is ineffective at emptying the bladder completely. They have recurrent UTIs that are afebrile or associated with a low-grade temperature, and they may have concomitant constipation.

DSD is inappropriate contraction of the external urethral sphincter during bladder contraction, causing an intermittent or staccato type of voiding and PVR. DSD often is associated with constipation or encopresis due to failure of the pelvic floor to relax during defecation. DSD is distinguished by recurrent UTI, postvoid leakage, and a classic "spinning-top urethra" (widened posterior urethra and bladder neck narrowing to a voluntarily contracted external sphincter) on VCUG. Affected children are at risk for acquired or secondary vesicoureteral reflux (VUR).

Hinman syndrome is the most severe form of voiding dysfunction. Originally this entity was described by Hinman as a nonneurogenic neurogenic bladder because affected children often had bladder and renal characteristics similar to children who had spina bifida, but with no identifiable neurologic defect. Children who have Hinman syndrome have longstanding DSD that can lead to detrusor decompensation. They develop bladder trabeculation, acquired VUR, hydronephrosis, and reflux nephropathy. Hinman syndrome, if not detected and treated aggressively with mechanisms to empty the bladder, leads to renal insufficiency or chronic renal failure.

Other Types of Daytime Wetting

Two types of daytime wetting do not qualify as either storage or emptying problems: giggle incontinence and vaginal reflux.

Giggle incontinence is a very rare form of daytime wetting described as complete bladder emptying with extreme laughter. This condition occurs almost exclusively in females ages 10 to 20 years. The disorder seems to be worse in the early teens, but does extend into adulthood. True giggle incontinence does not have other associated voiding abnormalities such as urgency or frequency. Urodynamics show a normal filling and emptying pattern. The cause is unknown, but the incontinence is believed to be mediated by a cataplectic phenomenon that exists in patients who have narcolepsy. As

a result, patients usually are treated successfully with methylphenidate.

Vaginal reflux is dribbling associated with urine being trapped in the vaginal introitus after voiding and leaking out when the child walks away. This condition often is seen in overweight girls and in young thin girls who cannot balance themselves on the toilet. Vaginal reflux also may be seen in girls who have vaginal adhesions. The underwear is described as "always damp." Diagnosis is made by a postvoid vaginal examination with a Valsalva maneuver that elicits urine flow from the introitus. Because this is primarily a problem of positioning, it is treated easily by having the patient sit backward on the toilet or concentrate on keeping the thighs separated during voiding.

Therapy for Storage and Emptying Problems

Behavioral therapy ultimately is the best treatment for daytime wetting, regardless of cause. One element consists of encouraging the child to void every 2 hours. Double voiding also is encouraged, especially for patients who have emptying problems. Patients are advised to avoid known bladder irritants such as caffeinated and carbonated beverages, high citrus-content beverages, and artificial red dyes. Also, patients should be encouraged to sit on the toilet 30 minutes after a large meal with

Table. **Medication for Treating Daytime Wetting and Nocturnal Enuresis**

Drug	Available Dosage	Advantages	Adverse Effects	Precautions
Hormonal Agents (nocturnal enuresis) Desmopressin acetate, vasopressin, DDAVP	0.1-, 0.2-mg tablets (0.1 to 0.6 mg qhs)	• Reduces the volume of urine made at night • FDA approved for patients >6 years of age	Water intoxication and hypernatremia	Hypertension and von Willebrand disease
Tricyclic Antidepressant (nocturnal enuresis) Imipramine	25-,50-, and 75-mg tablets (25 to 50 mg qhs <12 years of age and up to 75 mg qhs >12 years of age)	• Reduces uninhibited bladder contractions • May increase DDAVP concentrations • FDA approved for patients >6 years of age	Arrhythmias, hypotension, and electrocardiographic changes	• Narrow-angle glaucoma • Use with monoamine oxidase inhibitors and selective serotonin reuptake inhibitors must be avoided
Anticholinergic Agents (daytime and nocturnal enuresis) Oxybutynin	5-, 10-, and 15-mg extended-release tablets q day Elixir 0.15 mg/kg tid Transdermal patch 3.9 mg/day	• Reduces uninhibited bladder contractions • Extended-release tablets approved for patients >6 years of age • Elixir approved for pediatric use	Dry mouth, facial flushing, constipation	• Narrow-angle glaucoma, obstructive uropathy • Tablets cannot be crushed or chewed • Transdermal patch not FDA-approved for pediatric use
Tolterodine tartrate	2, 4 mg q day	• Reduces uninhibited bladder contractions • Does not cross blood-brain barrier • Capsules can be sprinkled on food	Dry mouth, facial flushing, constipation	• Narrow-angle glaucoma, obstructive uropathy • Not FDA-approved for pediatric use
Alpha Blockers (daytime enuresis) Doxazosin	1, 2 mg; begin with 0.5 mg and increase over 4 weeks to 1 mg q day	• Reduces bladder outlet resistance • Lowers postvoid residual	Headache, dizziness	• Contraindicated in renal impairment • May cause hypotension • FDA-approved for pediatric use
Tamsulosin	0.4 mg q day	• Reduces bladder outlet resistance • Lowers postvoid residual	Headache, dizziness	• Contraindicated in renal impairment • May cause hypotension • Not FDA-approved for pediatric use

FDA=United States Food and Drug Administration

their feet supported for 10 minutes to encourage pelvic floor relaxation.

A bowel program is extremely important in treating children who have daytime wetting because most of these patients have some form of constipation. First-line treatment for constipation includes diet changes that incorporate high-fiber foods. If the response to this is poor or marginal, medication may be needed, such as polyethylene glycol powder, with adjustments as needed until a daily medium-size, soft-formed stool is achieved. If a bowel program and behavioral therapy are ineffective, other medication may be necessary to help manage the problem.

If the patient has a storage problem that is associated with urinary frequency (not benign) or suprapubic or penile pain, anticholinergic agents are necessary. Six choices currently are available (Table), although most are not approved for pediatric use. However, we have used some of them successfully, with parental consent, in our dysfunctional voiding clinic. Adverse effects are essentially the same for all anticholinergic drugs and include, in order of occurrence, dry mouth, constipation, and facial flushing. Anticholinergic drugs that we have used successfully include oxybutynin and tolterodine.

Patients who have emptying problems have different needs and, therefore, different treatments. Biofeedback essentially is pelvic floor physical therapy for patients who have emptying problems, particularly DSD. The therapy involves contacts on either side of the anus and on the abdomen that are connected to a computer program that teaches the patient the difference between contraction and relaxation of the pelvic floor. The advantages of this therapy are that it is noninvasive, is very effective, and has no drug adverse effects. Disadvantages include slow resolution and the need for dedicated nursing care, parent and patient motivation, and frequent office visits as well as execution at home.

Medical treatments for emptying-based daytime wetting are alpha-blocking drugs, which originally were prescribed for men who had enlarged prostates. The agents appear to work by causing smooth muscle relaxation at the base of the bladder and reducing outlet resistance at the proximal sphincter complex, thereby lowering PVR. Alpha-blocking drugs lower PVR in up to 88% of patients. The advantages include fewer recurrent UTIs due to better emptying. Disadvantages include adverse effects such as headache and dizziness. We use two types of alpha-blockers in our practice: doxazosin (approved for treatment of hypertension in children) and tamsulosin (not approved for children). Anticholinergic drugs also are used in patients who have emptying problems because of the complexity of the symptomatology. Such medications help to alleviate the symptoms of urgency and frequency and control the severity of the incontinence.

Summary

Day and nighttime wetting is a significant problem in pediatrics. It is extremely common and often underdiagnosed. Parents frequently feel helpless because they think there is no solution and, therefore, may not raise the issue with their pediatricians. It is important for the pediatrician to ask the appropriate questions at health supervision visits to ascertain the presence of such problems. Diagnosis and treatment should be tailored in a stepwise approach to minimize the overuse of laboratory and other tests. Referrals should be considered for patients who are recalcitrant to initial therapy.

References

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Summary Tables: Differential Diagnosis of Enuresis

Table 1. Types of Enuresis

Type	*Characteristics*
Primary enuresis (80 percent of cases)	Enuresis in a child who has never established urinary continence for more than six months
Secondary enuresis (20 percent of cases)	Resumption of enuresis after at least six months of urinary continence
Nocturnal enuresis	Enuresis that occurs during sleep
Daytime wetting	Urinary incontinence that occurs while the child is awake
Monosymptomatic (uncomplicated) enuresis	Enuresis without lower urinary tract symptoms other than nocturia and no history of bladder dysfunction
Nonmonosymptomatic enuresis	Enuresis with lower urinary tract symptoms (e.g., increase or decrease in voiding frequency, daytime wetting, urgency, hesitancy, straining, weak or intermittent stream, posturination dribbling, holding maneuvers,* sensation of incomplete emptying, lower abdominal or genital discomfort)

NOTE: *Enuresis is the repeated, spontaneous voiding of urine during sleep in a child five years or older.*

**—Standing on the tiptoes, crossing the legs, or squatting with the heel pressed into the perineum ("curtsy sign").*

Information from references 1 and 2.

Table 2. Factors Associated with and Contributing to Enuresis

Factor	*Description*
Bladder function[8]	Decreased functional bladder capacity; inability to hold urine at night
Detrusor instability[8,9]	Lack of arousal to bladder distention and uninhibited bladder contractions (occurs in a small subgroup of children)
Genetic factors[10,11]	Increased incidence of enuresis in children if one or both parents have a history of enuresis; in the case of twins, both children are usually affected
Maturation delay[2,8]	Delay in central nervous system maturation and in the development of language and motor skills
Nocturnal polyuria[8]	Decreased nocturnal secretion of antidiuretic hormone causes nocturnal polyuria; blunted response to antidiuretic hormone
Psychological factors[2,8,12]	Not common with primary nocturnal enuresis; more common with secondary enuresis; considered a regressive symptom in response to stress or trauma (e.g., parental divorce, sexual abuse, trauma at school, hospitalization, neglect)
Sleep disorders[9]	Enuresis occurs in all stages of sleep; an abnormally deep sleep pattern may occur in children with enuresis

NOTE: *Several factors may contribute to primary nocturnal enuresis.*

Information from references 2, and 8 through 12.

Table 3. Precipitating Conditions Associated with Secondary Enuresis

Bladder dysfunction	Obstructive sleep apnea
Chronic renal failure*	Pinworm infection
Constipation	Psychological stress
Diabetes insipidus*	Seizure disorder*
Diabetes mellitus	Sickle cell disease*
Hyperthyroidism	Urinary tract infection

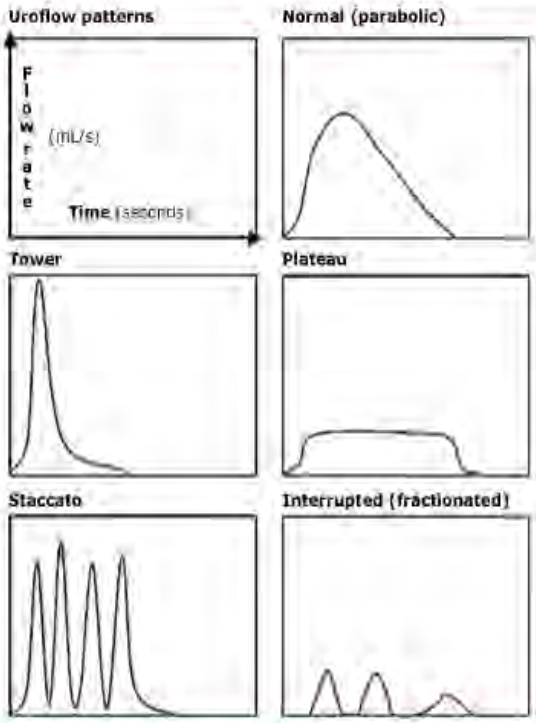
**—Rare in children.*

Information from references 2 and 6.

Summary Tables: DDx, *continued*

TABLE 3. Causes of Daytime Wetting in Childhood
• Holding the urine to the last minute
• Urinary tract infection
• Constipation
• Vaginal reflux of urine
• Labial fusion
• Postvoid dribble syndrome
• Daytime frequency syndrome
• Giggle incontinence
• Stress incontinence
• Emotional stress
• Urge syndrome
• Neurogenic bladder
• Urethral obstruction
• Ectopic ureter
• Diabetes mellitus
• Diabetes insipidus

Normal and abnormal urinary flow patterns



Abnormal urine flow patterns can be helpful in identifying underlying causes of voiding dysfunction. A tower curve pattern may be seen in patients with an overactive bladder, a plateau curve in patients with bladder obstruction, a plateau or staccato curve in patients with dysfunctional voiding, and an interrupted curve in patients with an underactive bladder.

Urodynamic patterns in normal and abnormal conditions

	Filling phase		Voiding phase	
	Detrusor contractions	**Sphincter activity**	**Detrusor contractions**	**Sphincter activity**
Normal	Absent	Present	Present	Absent
Abnormalities identified on urodynamic testing				
Overactive bladder	*Present*	Present	Present	Absent
Detrusor sphincter dyssynergy	Absent	Present	Present	*Present*
Non-neurogenic dysfunctional voiding	Absent	Present	Present	*Present*
Underactive bladder	*Absent, large capacity bladder*	Present	*Inadequate, incomplete emptying*	Absent

Summary Tables: Evaluation of Enuresis

Table 4. Evaluation of Children with Enuresis

Diagnostic approach	*Components*
History (enuresis-specific)	Age at onset of enuresis, duration and severity of enuresis, duration of continence (enuresis is not diagnosed in children younger than five years; recurrence after at least six months of urinary continence suggests secondary enuresis)[1,2]
	Presence of lower urinary tract symptoms* (symptoms other than nocturia suggest nonmonosymptomatic and secondary enuresis)[1]
	History of medical illness (e.g., diabetes mellitus, sleep apnea) may suggest nonmonosymptomatic enuresis[6]
	Psychosocial history (psychological disturbances are present in one third of patients with secondary enuresis)[8]
	Family history of enuresis (the condition is more common in patients with a family history; in the case of twins, both children are usually affected)[2,10,11]
	Fluid-intake diary, bladder and stooling diary, frequency/volume chart (records help assess constipation, enuresis severity, and treatment response)[2,8]
	Investigation and treatment history
	Red flags: dysuria, genital or rectal pain or discharge, straining to urinate, combined diurnal and nocturnal frequency with enuresis (suggests nonmonosymptomatic enuresis)
Physical examination[2,6,8,17]	Ears, nose, and throat examination to detect adenotonsillar hypertrophy
	Abdominal examination to detect enlarged bladder or kidneys and fecal masses indicating encopresis
	Genital examination to detect hypospadias or epispadias, meatal stenosis, ectopic ureter, and labial adhesions
	Rectal examination to evaluate perianal and perineal sensation and rectal sphincter tone and to detect perianal excoriation and vulvovaginitis
	Focused neurologic evaluation, including gait, muscle tone, strength, and perineal sensation
	Red flags (indicate need for further investigation): adenotonsillar hypertrophy, spinal pathology (deformity, sacral dimple or hair tuft suggesting underlying spinal dysraphism), motor sensory loss and abnormal tendon reflexes in the lower limbs, enlarged bladder or kidneys, abnormal gait, signs of sexual abuse
Urinalysis, urine culture†[6]	Detection of urinary tract infection, diabetes mellitus, diabetes insipidus
Blood count, serum chemistry†[6]	Blood urea nitrogen and serum creatinine levels to detect chronic renal failure, serum glucose levels to detect diabetes, hemoglobin electrophoresis to detect sickle cell disease, serum thyroid-stimulating hormone level to detect hyperthyroidism
Imaging studies†[2,6,8]	Renal and bladder ultrasonography and voiding cystourethrography for a suspected structural abnormality, significant daytime wetting, or recurrent urinary infections to detect vesicoureteral reflux
	Magnetic resonance imaging of the lumbosacral spine for suspected spinal dysraphism or abnormal neurologic examination findings
Urodynamic studies†[2,8]	Measurement of residual urine and cystometry to evaluate bladder dysfunction (dysfunctional voiding)

*—Nocturia, urgency, daytime wetting, squatting, incontinence, constipation.
†—Required only if secondary causes are suspected, red flags are detected on history or examination, or the patient does not respond to standard treatment.

Information from references 1, 2, 6, 8, 10, 11, and 17.

Summary Tables: Management of Enuresis

Table 5. Treatment Options for Enuresis

Treatment	*Indication and use*	*Effectiveness*	*Adverse effects*
Nonpharmacologic*			
Motivational therapy[17,19-22]	Younger children with primary nocturnal enuresis Provides reassurance and emotional support, eliminates guilt, rewards continence (e.g., star or sticker charts)	Partial response in 75 percent of children; relapse in 5 percent of children	Frustration; reward system may worsen self-esteem if the child fails to have dry nights
Bladder training[17,22]	Younger children with primary nocturnal enuresis Postpones voiding for longer periods	Minimal improvement	None
Dry-bed training[17,23]	Younger children with primary nocturnal enuresis Includes waking children to void at specified intervals	Minimal improvement	Sleep deprivation
Enuresis alarm[2,17,19,24]	Older, motivated children with primary nocturnal enuresis Awakens child in response to an alarm triggered by wetness	Effective in two thirds of children; dryness persists in 50 percent of children who continue to use the alarm	Sleep deprivation
Biofeedback[25]	Older, motivated children with primary nocturnal enuresis and dysfunctional voiding Training for pelvic floor muscle relaxation	Primary nocturnal enuresis: 81 percent effective Lower urinary tract symptoms: 77 to 81 percent effective Constipation: 73 percent effective Daytime wetting: 58 percent effective	None
Pharmacologic†			
Oral imipramine (Tofranil), 25 to 75 mg daily[2,19,20,26,27] Oral desipramine (Norpramin), 1 to 3 mg per kg daily	Children with primary nocturnal enuresis	40 to 60 percent effective; response occurs within days; most patients relapse after discontinuing treatment	Drowsiness, gastrointestinal upset, seizures, arrhythmia, overdose, lethargy, agitation, depression, sleep disturbance
Oral oxybutynin (Ditropan), 2.5 to 5 mg three times daily[8,17,28,29]	Children with urge incontinence or primary nocturnal enuresis and diurnal incontinence	47 to 71 percent effective; better response if combined with desmopressin (DDAVP)	Dry mouth, blurred vision, constipation, dizziness, tachycardia, headache, nausea, gastrointestinal upset
Oral desmopressin, 0.2 to 0.6 mg daily Intranasal desmopressin, 10 to 40 mcg daily[2,8,30-35]	Children with primary nocturnal enuresis	60 to 70 percent effective; response occurs within days; 80 percent of patients relapse after discontinuing treatment	Headache, nasal congestion, epistaxis, sore throat, abdominal cramps, water intoxication, allergic reaction, hyponatremia, anorexia, nausea, visual disturbance, bad taste in the mouth

NOTE: *Children who do not respond to one or more measures may benefit from combined treatment strategies (e.g., combining nonpharmacologic and pharmacologic treatment or multiple pharmacologic therapies).*

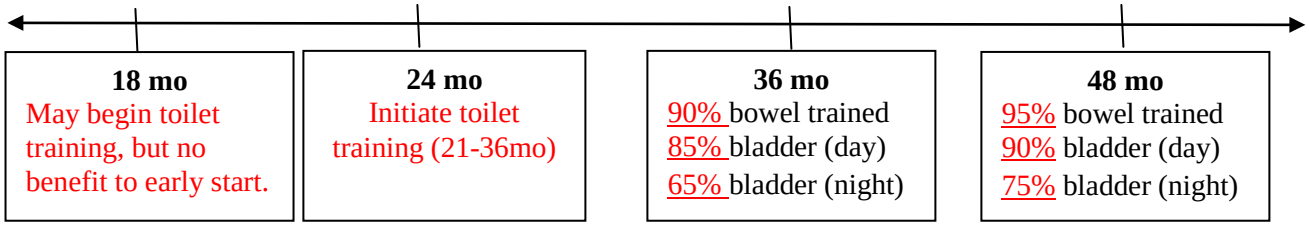
**—Generally first-line treatments that should be attempted before pharmacologic therapy; treatments may be combined; requires significant parental involvement.*

†—*Of these therapies, only imipramine and oral desmopressin have been approved by the U.S. Food and Drug Administration for the treatment of enuresis in children. Indicated in children seven years and older.*

Information from references 2, 8, 17, and 19 through 35.

Enuresis Quiz

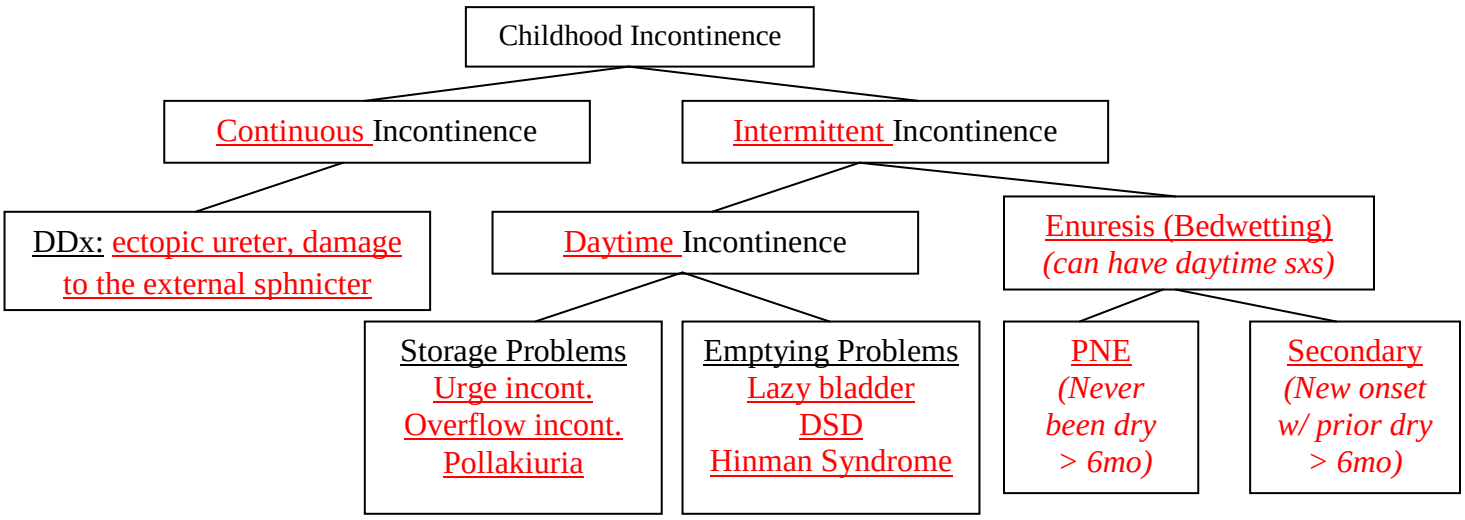
1A. ***Flashback:*** Complete the following **toilet-training timeline** *(%iles from BRS, 2005)*:



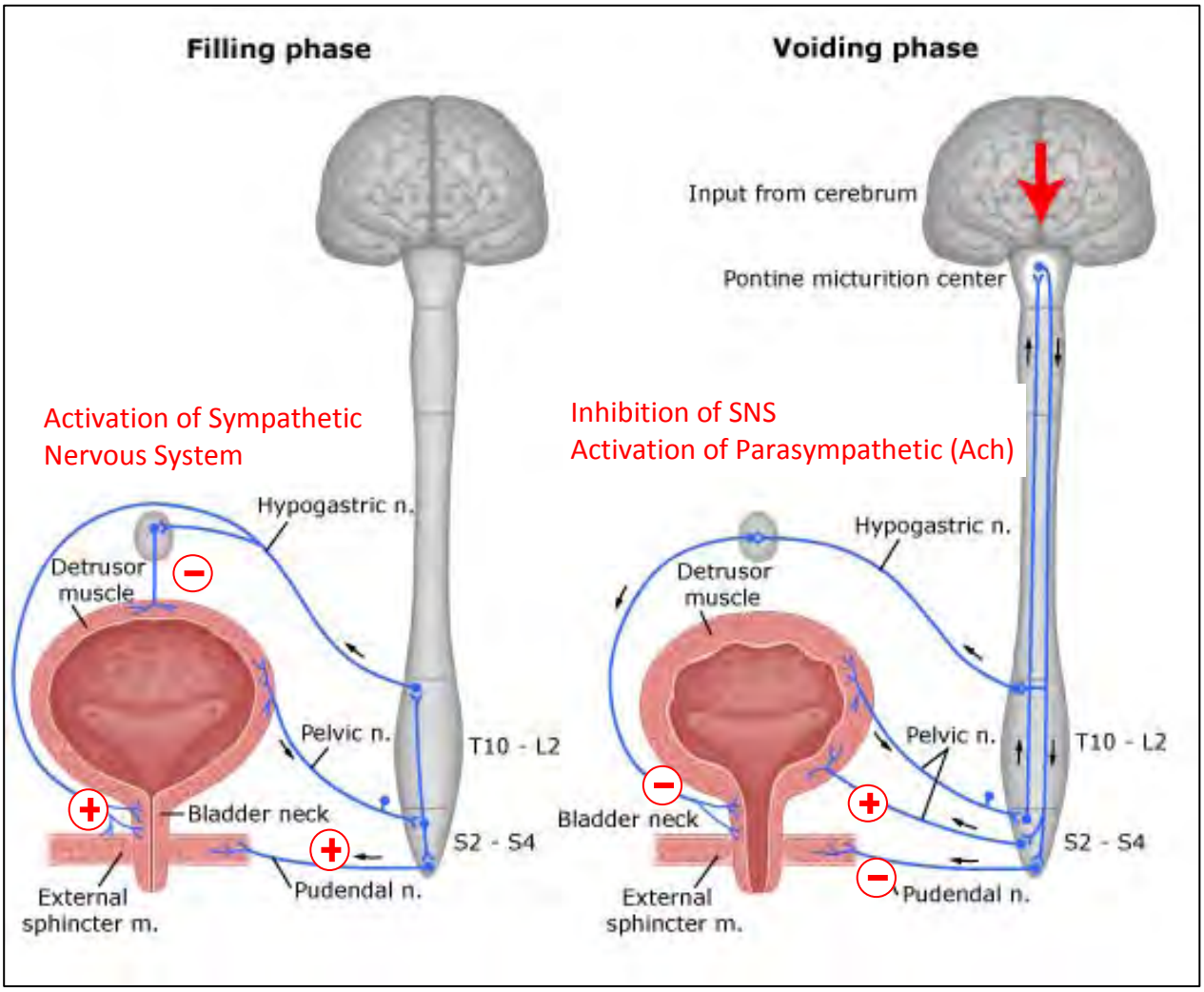
1B. What percent of 7-year-old children struggle with **bedwetting**? **10-15%**

1C. What percent of 7-year-old children struggle with **daytime wetting**? **2-3% boys; 3-4% girls**

2. Complete the following **classification tree for incontinence** (based on ICCS classification):



3A. Fill in the following diagram to reflect the **normal micturition cycle**:



Filling of the bladder & urine storage at low pressure with high outlet resistance

Voiding with low outlet resistance and sustained detrusor contraction.

Bladder stretching activates mechanoreceptors, which send an ascending signal through the spinal cord to the pontine micturition center. A descending signal through the spinal cord results in inhibition of the SNS and activation of the PSNS.

3B. Using this diagram as a guide, explain **destrusor sphincter dyssynergia (DSD)**:
DSD is *inappropriate* contraction of the external sphincter during bladder contraction (+ sign, instead of – sign at site of bladder neck innervation). This causes staccato voiding and PVR.

3C. Using this diagram as a guide, explain **"lazy bladder syndrome"**:
Voiding postponement leads to increasing bladder capacity. With over-distension of the bladder, the detrusor muscle becomes overstretched, leading to weak contraction and underactive bladder. This causes an interrupted urinary flow pattern, large PVR, and overflow incontinence.

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 PNE. 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? OSA or insomnia? Neurologic disorders? Developmental delay? ADHD?
- **FamHx:** Were any of the parents or siblings bed-wetters?

Luke's mother reports that he was potty-trained at the CDC "when it was his turn" around age 3. He has never been dry at night, however, and has always worn pull-ups to bed. He wets the bed 2-3 nights per week, and mother is unsure of how many episodes per night. Sometimes, he will awaken in the early morning hours crying about being wet, but more often, his mother will find him with a completely saturated pull-up when she wakes him up for pre-school at 0700.

In an attempt to decrease Luke's bedwetting, Mother reports that they have cut out all fluids after 1700, require him to sit on the potty before going to bed at 2000, and have even tried waking him up every 4 hours at night to try to "catch it". Luke's mother says that she has been patient with him, but admits that his father has been visibly frustrated that "his only son is a bed-wetter".

Luke is otherwise healthy, except for the occasional "preschool crud". There is no history of intermittent or constant daytime wetness, dysuria, polyuria, or polydipsia. His development has been normal. Family history is significant, Mother admits with a smile, for Luke's father being a bed-wetter until age 11.

What is the significance of Luke's father being a bed-wetter?
Studies have shown that when 1 parent had enuresis as a child, his or her child has a **44% chance** of also experiencing the condition. If both parents are affected, this chance is **77%.**

What will you focus on for your exam?

- GI: distended bladder? Fecal impaction?
- Urogenital: evaluation of the phallus and meatus
- Neurologic: LE muscle tone and coordination, DTRs, sensation; sacral dimple/tuft

Luke's exam was 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 S1and 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 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?
PNE = 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 PNE 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 14% 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 6 months and then stop for 2 weeks 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 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? (*Flashback: Sleep Disorders, Development II & IV, Behavior II, Constipation)*

OSA, 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, per mom". You learn that Holly was seen in the ER last night for a UTI, diagnosed based on urinary frequency, urgency, dysuria, and a clean-catch specimen U/A positive for nitrites and leukocyte esterase. She was started on Bactrim and is feeling better today. Her parents are concerned, however, because this is her 3rd or 4th UTI in the last year.

What else do you want to know?

- Any history of structural or functional urinary tract abnormalities (i.e. on U/S or VCUG)?
- Any other medical problems? Constipation? Neurologic dysfunction? Psychiatric issues?
- Toilet training history? Current toileting and hygiene practices?
- Family history of urinary tract abnormalities or recurrent UTIs?

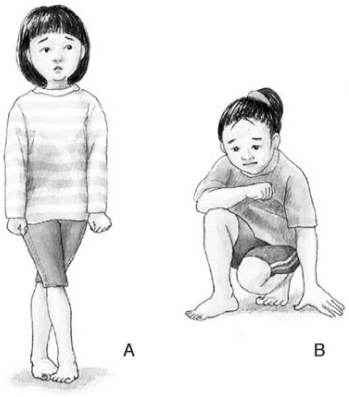
Holly's father takes her out of the room, while her mother tells you that Holly has struggled with daytime and nighttime wetting since they started potty-training at age 2. She has never had a dry period and usually wears pull-ups. Her PMHx is significant for ADHD, managed behaviorally. Mother denies a history of constipation. She has never had any imaging for her UTIs, 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 (a.k.a. diurnal enuresis). 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, or 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 is an aggravating factor for enuresis,** particularly urge syndrome. It is possible that the pressure effect of stool in the descending or sigmoid colon can trigger an uninhibited destrusor contraction.

What further work-up, if any, will you recommend? ± *Referral to Peds Urology*

- Repeat U/A, UCx after completion of current antibiotic course.
- Bladder U/S for post-void residual (PVR) and bladder wall thickness.
- Uroflowmetry for uro-flow pattern.
- VCUG and/or Urodynamics

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 anti-cholinergic (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 mcmol/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.