Current PSYCHIATRY

CASES THAT TEST YOUR SKILLS

Chronic enuresis has destroyed 12-year-old Jimmy's emotional and social functioning. The challenge: restore his self-esteem by finding out why can't he stop wetting his bed.

The boy who longed for a 'dry spell'

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HISTORY 'I CAN'T FACE MYSELF'

Jimmy, age 12, is referred to us by his pediatrician, who is concerned about his "frequent nighttime accidents." His parents report that he wets his bed 5 to 6 times weekly and has never stayed consistently dry for more than a few days.

The accidents occur only at night, his parents say. Numerous interventions have failed, including restricting fluids after dinner and awakening the boy overnight to make him go to the bathroom.

Jimmy, a sixth-grader, wonders if he will ever stop wetting his bed. He refuses to go to summer camp or stay overnight at a friend's house, fearful that other kids will make fun of him after an accident. Asked how "wet nights" are affecting his life, he says, "I can't face myself in the mirror."

The authors' observations

Primary nocturnal enuresis is diagnosed in children age ≥ 5 who have never gone 6 consecutive months without an overnight accident. Pediatricians generally discover enuresis incidentally during regular checkups and refer to a psychiatrist only if the child has an emotional problem secondary to enuresis or a comorbid psychiatric disorder.

Once identified, enuresis requires a thorough assessment—including its emotional consequences, which for Jimmy are significant. In its practice parameter for treating enuresis, the American Academy of Child and Adolescent Psychiatry (AACAP)[1] suggests that you:

Take an extensive developmental and family history. Find out if the child was toilet trained and started walking, talking, or running at an appropriate age. Delays in reaching developmental milestones can predict enuresis.[1]

Also find out if either parent had enuresis during childhood. Enuresis is heritable,[2] and children often outgrow the problem at the same age as did the parent(s).

Focus on the bedwetting and the child's reaction to it. Treat enuresis aggressively if it is hurting the child's performance at school, social or emotion-

How would you handle this case?

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al development, or self-esteem, or if the youth appears emotionally withdrawn or distressed.

Interview the child and parents separately, as each often reacts differently to the problem. In some cases, for example, the child's bedwetting upsets the parents but the child hardly seems to care. Also, children often feel more at ease talking to a doctor alone, and parents can vent frustration without upsetting their child.

While interviewing the child, listen for psychosocial stressors that can lead to enuresis, such as parents' marital problems, problems at school, recent hospitalization, physical or sexual abuse, or the recent birth of a sibling.

We spend about one half-hour with the child and another half-hour with the parents to thoroughly gauge enuresis' emotional impact. To engage the child and hold his attention during that half-hour, we offer toys or play a game.

Consider physical causes, emotional stressors, and developmental delays when assessing enuresis

Check for physical causes. According to the AACAP practice parameter for enuresis treatment, you should:

- assess nare patency and voice quality to rule out enlarged adenoids
- check the nasal pharynx for enlarged tonsils
- palpate the abdomen to check for bladder distention or fecal impaction
- examine genitalia for abnormalities
- view the back for a sacral dimple or other sign of a vertebral or spinal cord anomaly.

Also order a thorough neurologic examination to rule out subtle dysfunction associated with enuresis.[1]

Perform a urinalysis and urine culture to rule out urinary tract infection (UTI).

Order urodynamic studies or renal ultrasound if enuresis persists after two unsuccessful treatment trials, the physical examination uncovers positive findings, or the child has had a UTI.

Psychotherapy has a limited role in treating primary enuresis unless you suspect a psychological cause.[1] We offered Jimmy supportive counseling to help alleviate emotional problems caused by bedwetting. He and his parents declined but agreed to reconsider later.

FURTHER HISTORY TOILET TRAINED AT 2

Jimmy was toilet trained at age 2 and reached all other age-appropriate developmental milestones, his mother says. Results of urine culture, repeated urinalyses, and neurologic and physical examinations are normal. Neither Jimmy nor his family have a history of UTI, dysuria, urgency, or increased urination frequency.

When Jimmy was age 9, his pediatrician prescribed imipramine, 25 mg/d, to try to stop his bedwetting. He did not respond after 6 months, so his parents stopped giving the drug to him.

A few months later, Jimmy's parents heard about a "bedwetting alarm" designed to condition children not to urinate while asleep, but the boy and his parents viewed this treatment as "humiliating" and refused to try it. They have not attempted another intervention for 2 years.

How would you help Jimmy?

a) urge the family to try the bedwetting alarm
b) prescribe imipramine at a higher dosage
c) try another medication
d) try a different behavioral treatment

The authors' observations

Having found no medical or psychological basis for Jimmy's enuresis (*Box*), we pondered our next clinical move.

Behavioral interventions. Parents commonly try to stop their child's bedwetting by restricting his or her fluid or caffeine intake, enforcing a reward system, bladder control training, and/or awakening the child overnight to go to the bathroom.

Among behavioral treatments, only the bedwetting alarm has shown effectiveness in clinical trials,[1,3] and it carries the lowest risk of post-treatment relapse.[3] Urine moistens a sensor in the bed pad or inside cloth, triggering an alarm that awakens the child when wetting starts. The child gradually awakens earlier in an enuretic episode until the sensation of bladder fullness awakens him.

Many parents/guardians and their children—particularly older youths—consider alarm systems demeaning. We again suggested this treatment to Jimmy and his parents, but they refused.

Medication. Six months of low-dose imipramine, a tricyclic antidepressant often prescribed for enuresis, produced no response. We did not restart imipramine at a higher dosage because of its association with increased arrhythmia risk.

We instead considered desmopressin acetate, a synthetic analog of ADH vasopressin that regulates diurnal variation, which is usually abnormal in children with enuresis. Desmopressin, often used to treat clozapine-induced enuresis in adults, has been associated with successful outcomes in as many as 65% of children in clinical trials.[1,4]

Desmopressin, however, can reduce urine production. Water intoxication or hyponatremia is rare but can lead to seizures or coma, and the risk increases with the dosage. Obtain informed consent from the parents before starting this drug. Check electrolytes 2 or 3 days after the first dose, 1 month later, then again every 2 to 3 months. Discontinue at once if serum sodium decreases significantly from baseline or is <135 mmol/L.

Box

Enuresis: Possible causes

Genetics. In more than one-half of children with enuresis, one or both parents had the disorder during childhood.

Developmental delay. Delayed functional CNS maturation can decrease arousal. Enuresis is common in children with developmental disorders, including autism, Rett's syndrome, or pervasive developmental disorder NOS.

Irregular sleep pattern associated with specific sleep disorders, such as narcolepsy and sleep apnea. Also, children with enuresis sleep more soundly than do youths without the disorder.

Psychological problem. Considered a reaction to primary enuresis rather than its cause.

Medical condition. Enlarged adenoids, tonsils, constipation with fecal impaction, vertebral and spinal cord anomaly, and diabetes mellitus may cause enuresis.

Source: Reference 1

TREATMENT MEANINGLESS RESPONSE

We start Jimmy on oral desmopressin, 0.2 mg at bedtime, after discussing its benefits and risks with his parents. We increase the dosage to 0.4 mg after 3 days and to 0.6 mg the following week, as the lower dosages have not worked. Serum electrolytes, gauged before starting desmopressin and again 2 weeks later, are normal. We see Jimmy every 2 weeks to check progress and monitor for side effects.

Soon after the second dosage increase, Jimmy's accidents gradually decrease to 2 to 3 per week, but no improvement is seen after that.

Two months later, Jimmy is still avoiding sleepovers and has trouble making friends. His parents worry about his increasing frustration, hopelessness, and low self-esteem. We again offer supportive counseling, but the boy refuses.

continued

Table

Medication strategies for treating enuresis

Medication	Dosage	Risks
Desmopressin acetate (first-line)	Start with 0.2-mg tablet or 1 to 2 10-µg puffs of nasal spray (half in each nostril) in children age >6; increase to 0.6 mg/d or 4 puffs daily after 1 week if necessary Stop after approximately 6 months without an accident	High relapse rate Reduced urine production Water intoxication, hyponatremia are rare but can result in seizures, coma
Oxybutynin (second-line)	2.5 to 5 mg tid (immediate-release) or 15 mg/d (extended-release) Start at 5 mg at bedtime for children age >5; increase to 15 mg/d after 1 to 2 weeks if needed Stop after approximately 6 months without an accident	High relapse rate Anticholinergic effects (dry mouth, facial flushing, drowsiness, decreased GI motility) Few efficacy studies done Mostly used with other medication
Desmopressin with oxybutynin or imipramine; medication plus alarm method (third-line)	Dosages of individual medications as listed	Limited data available Positive results seen in resistant cases, particularly in older children
Imipramine (last option)	1 to 2.5 mg/kg/d Start with 25 mg/d at bedtime; if no response, increase in weekly 25-mg increments to 50 mg/d for children ages 7 to 12 or up to 75 mg/d for children age >12 Stop after approximately 6 months without an accident	High relapse rate after stopping medication Risk of arrhythmias (order ECG when starting medication, 1 month later, then every 6 months) Fatal in overdose (do not prescribe >75 mg/d in enuresis) Associated with suicidal behavior in youths (carries FDA "black box" warning)

How would you address Jimmy's bedwetting now?

a) increase desmopressin dosage

b) try another medication

c) try desmopressin with another medication

d) test again for underlying physical problem

The authors' observations

We were running out of treatment options. Two medication trials failed, and the family still would not try a bedwetting alarm.

Urodynamic testing usually is not ordered unless the child has a history of urge incontinence or UTI. For some treatment-resistant patients, the

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vasodilatation, thinking abnormal, decreased libido, and sweating. ***Commonly Observed Adverse Events in Controlled Clinical Trials for MDD, GAD, SAD, and PD***—Body as a Whole: asthenia, headache, flu syndrome, accidental injury, abdominal pain. Cardiovascular: vasodilatation, hypertension, palpitation. Digestive: nausea, constipation, anorexia, vomiting, flatulence, diarrhea, eructation. Metabolic/Nutritional: weight loss. Nervous System: dizziness, somnolence, insomnia, dry mouth, nervousness, abnormal dreams, tremor, depression, hypertonia, paresthesia, libido decreased, agitation, anxiety, twitching. Respiratory System: pharyngitis, yawn, sinusitis. Skin: sweating. Special Senses: abnormal vision. Urogenital System: abnormal ejaculation, impotence, orgasmic dysfunction (including anorgasmia) in females. ***Vital Sign Changes***: Effexor XR was associated with a mean increase in pulse rate of about 2 beats/min in depression and GAD trials and a mean increase in pulse rate of 4 beats/min in SAD trials. (See **WARNINGS-Sustained Hypertension**). ***Laboratory Changes***: Clinically relevant increases in serum cholesterol were noted in Effexor XR clinical trials. Increases were duration dependent over the study period and tended to be greater with higher doses. ***Other Events Observed During the Premarketing Evaluation of Effexor and Effexor XR***—N=6,670. "Frequent"=events occurring in at least 1/100 patients; "infrequent"=1/100 to 1/1000 patients; "rare"=fewer than 1/1000 patients. **Body as a whole** - Frequent: chest pain substernal, chills, fever, neck pain; Infrequent: face edema, intentional injury, malaise, moniliasis, neck rigidity, pelvic pain, photosensitivity reaction, suicide attempt, withdrawal syndrome; Rare: appendicitis, bacteremia, carcinoma, cellulitis. **Cardiovascular system** - Frequent: migraine, postural hypotension, tachycardia; Infrequent: angina pectoris, arrhythmia, extrasystoles, hypotension, peripheral vascular disorder (mainly cold feet and/or cold hands), syncope, thrombophlebitis; Rare: aortic aneurysm, arteritis, first-degree atrioventricular block, bigeminy, bundle branch block, capillary fragility, cerebral ischemia, coronary artery disease, congestive heart failure, heart arrest, hematoma, cardiovascular disorder (mitral valve and circulatory disturbance), mucocutaneous hemorrhage, myocardial infarct, pallor, sinus arrhythmia. **Digestive system** - Frequent: increased appetite; Infrequent: bruxism, colitis, dysphagia, tongue edema, esophagitis, gastritis, gastroenteritis, gastrointestinal ulcer, gingivitis, glossitis, rectal hemorrhage, hemorrhoids, melena, oral moniliasis, stomatitis, mouth ulceration; Rare: abdominal distension, biliary pain, cheilitis, cholecystitis, cholelithiasis, esophageal spasms, duodenitis, hematemesis, gastroesophageal reflux disease, gastrointestinal hemorrhage, gum hemorrhage, hepatitis, ileitis, jaundice, intestinal obstruction, liver tenderness, parotitis, periodontitis, proctitis, rectal disorder, salivary gland enlargement, increased salivation, soft stools, tongue discoloration. **Endocrine system** - Rare: galactorrhoea, goiter, hyperthyroidism, hypothyroidism, thyroid nodule, thyroiditis. **Hemic and lymphatic system** - Frequent: ecchymosis; Infrequent: anemia, leukocytosis, leukopenia, lymphadenopathy, thrombocythemia; Rare: basophilia, bleeding time increased, cyanosis, eosinophilia, lymphocytosis, multiple myeloma, purpura, thrombocytopenia. **Metabolic and nutritional** - Frequent: edema, weight gain; Infrequent: alkaline phosphatase increased, dehydration, hypercholesteremia, hyperglycemia, hyperlipemia, hypoglycemia, hypokalemia, SGOT increased, SGPT increased, thirst; Rare: alcohol intolerance, bilirubinemia, BUN increased, creatinine increased, diabetes mellitus, glycosuria, gout, healing abnormal, hemochromatosis, hypercalcinuria, hyperkalemia, hyperphosphatemia, hyperuricemia, hypocholesteremia, hyponatremia, hypophosphatemia, hypoproteinemia, uremia. **Musculoskeletal system** - Frequent: arthralgia; Infrequent: arthritis, arthrosis, bone spurs, bursitis, leg cramps, myasthenia, tenosynovitis; Rare: bone pain, pathological fracture, muscle cramp, muscle spasms, musculoskeletal stiffness, myopathy, osteoporosis, osteosclerosis, plantar fasciitis, rheumatoid arthritis, tendon rupture. **Nervous system** - Frequent: amnesia, confusion, depersonalization, hypesthesia, thinking abnormal, trismus, vertigo; Infrequent: akathisia, apathy, ataxia, circumoral paresthesia, CNS stimulation, emotional lability, euphoria, hallucinations, hostility, hyperesthesia, hyperkinesia, hypotonia, incoordination, manic reaction, myoclonus, neuralgia, neuropathy, psychosis, seizure, abnormal speech, stupor, suicidal ideation; Rare: abnormal/changed behavior, adjustment disorder, akinesia, alcohol abuse, aphasia, bradykinesia, buccoglossal syndrome, cerebrovascular accident, feeling drunk, loss of consciousness, delusions, dementia, dystonia, energy increased, facial paralysis, abnormal gait, Guillain-Barré syndrome, homicidal ideation, hyperchlorhydria, hypokinesia, hysteria, impulse control difficulties, libido increased, motion sickness, neuritis, nystagmus, paranoid reaction, paresis, psychotic depression, reflexes decreased, reflexes increased, torticollis. **Respiratory system** - Frequent: cough increased, dyspnea; Infrequent: asthma, chest congestion, epistaxis, hyperventilation, laryngismus, laryngitis, pneumonia, voice alteration; Rare: atelectasis, hemoptysis, hypoventilation, hypoxia, larynx edema, pleurisy, pulmonary embolus, sleep apnea. **Skin and appendages** - Frequent: pruritus; Infrequent: acne, alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, psoriasis, urticaria; Rare: brittle nails, erythema nodosum, exfoliative dermatitis, lichenoid dermatitis, hair discoloration, skin discoloration, furunculosis, hirsutism, leukoderma, miliaria, petechial rash, pruritic rash, pustular rash, vesiculobullous rash, seborrhea, skin atrophy, skin hypertrophy, skin striae, sweating decreased. **Special senses** - Frequent: abnormality of accommodation, mydriasis, taste perversion; Infrequent: conjunctivitis, diplopia, dry eyes, eye pain, hyperacusis, otitis media, parosmia, photophobia, taste loss, visual field defect; Rare: blepharitis, cataract, chromatopsia, conjunctival edema, corneal lesion, deafness, exophthalmos, eye hemorrhage, glaucoma, retinal hemorrhage, subconjunctival hemorrhage, keratitis, labyrinthitis, miosis, papilledema, decreased pupillary reflex, otitis externa, scleritis, uveitis. **Urogenital system** - Frequent: prostatic disorder (prostatitis, enlarged prostate, and prostate irritability), urination impaired; Infrequent: albuminuria, amenorrhea, breast pain, cystitis, dysuria, hematuria, kidney calculus, kidney pain, leukorrhea, menorrhagia, metrorrhagia, nocturia, polyuria, pyuria, urinary incontinence, urinary retention, urinary urgency, vaginal hemorrhage, vaginitis; Rare: abortion, anuria, balanitis, bladder pain, breast discharge, breast engorgement, breast enlargement, endometriosis, female lactation, fibrocystic breast, calcium crystalluria, cervicitis, orchitis, ovarian cyst, prolonged erection, gynecomastia (male), hypomenorrhea, kidney function abnormal, mastitis, menopause, pyelonephritis, oliguria, salpingitis, urolithiasis, uterine hemorrhage, uterine spasm, vaginal dryness. **Postmarketing Reports**: agranulocytosis, anaphylaxis, aplastic anemia, catatonia, congenital anomalies, CPK increased, deep vein thrombophlebitis, delirium, EKG abnormalities such as QT prolongation; cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia, ventricular extrasystoles, and rare reports of ventricular fibrillation and ventricular tachycardia, including torsades de pointes; epidermal necrosis/Stevens-Johnson syndrome, erythema multiforme, extrapyramidal symptoms (including dyskinesia and tardive dyskinesia), angle-closure glaucoma, hemorrhage (including eye and gastrointestinal bleeding), hepatic events (including GGT elevation; abnormalities of unspecified liver function tests; liver damage, necrosis, or failure; and fatty liver), involuntary movements, LDH increased, neuroleptic malignant syndrome-like events (including a case of a 10-year-old who may have been taking methylphenidate, was treated and recovered), neutropenia, night sweats, pancreatitis, pancytopenia, panic, prolactin increased, pulmonary eosinophilia, renal failure, rhabdomyolysis, serotonin syndrome, shock-like electrical sensations or tinnitus (in some cases, subsequent to the discontinuation of venlafaxine or tapering of dose), and SIADH (usually in the elderly). Elevated clozapine levels that were temporally associated with adverse events, including seizures, have been reported following the addition of venlafaxine. Increases in prothrombin time, partial thromboplastin time, or INR have been reported when venlafaxine was given to patients on warfarin therapy. **DRUG ABUSE AND DEPENDENCE**: Effexor XR is not a controlled substance. Evaluate patients carefully for history of drug abuse and observe such patients closely for signs of misuse or abuse. **OVERDOSAGE**: Electrocardiogram changes (e.g., prolongation of QT interval, bundle branch block, QRS prolongation), sinus and ventricular tachycardia, bradycardia, hypotension, altered level of consciousness (ranging from somnolence to coma), rhabdomyolysis, seizures, vertigo, liver necrosis, and death have been reported. Treatment should consist of those general measures employed in the management of overdosage with any antidepressant. Ensure an adequate airway, oxygenation and ventilation. Monitor cardiac rhythm and vital signs. General supportive and symptomatic measures are also recommended. Induction of emesis is not recommended. Gastric lavage with a large bore orogastric tube with appropriate airway protection, if needed, may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal should be administered. Due to the large volume of distribution of this drug, forced diuresis, dialysis, hemoperfusion, and exchange transfusion are unlikely to be of benefit. No specific antidotes for venlafaxine are known. In managing overdosage, consider the possibility of multiple drug involvement. Consider contacting a poison control center for additional information on the treatment of overdose. Telephone numbers for certified poison control centers are listed in the Physicians' Desk Reference® (PDR). **DOSAGE AND ADMINISTRATION**: Consult full prescribing information for dosing instructions. **Switching Patients to or From an MAOI**—At least 14 days should elapse between discontinuation of an MAOI and initiation of therapy with Effexor XR. At least 7 days should be allowed after stopping Effexor XR before starting an MAOI (see **CONTRAINDICATIONS** and **WARNINGS**). This brief summary is based on Effexor XR Prescribing Information W10404C019, revised November 2005.

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test can reveal detruser muscle or bladder capacity deficits that might be causing enuresis.

TESTING BELOW THE NORM

We refer Jimmy to a urologist for a urodynamic test. Results showed mild detruser muscle instability and slightly low maximum bladder capacity compared with age-predicted norms.

The authors' observations

Based on this finding, we considered oxybutynin, an anticholinergic agent that increases bladder control by relaxing the smooth muscles. Patients with detruser instability and inadequate bladder capacity have responded well to oxybutynin in clinical trials,[5,6] and combination oxybutynin/desmopressin therapy has been shown effective in treatment-resistant patients.[7-9]

Oxybutynin and desmopressin complement each other; reduced urinary output and bladder filling associated with desmopressin can reduce uninhibited bladder contractions, thus enhancing oxybutynin's action.

TREATMENT HAPPY SUMMER

We continue desmopressin, 0.6 mg nightly, and add extended-release oxybutynin, 2.5 mg/d. We increase oxybutynin to 5 mg/d after 3 days and to 10 mg/d the following week, as Jimmy reported no side effects from the lower dosages.

We see Jimmy 1 week after adding oxybutynin, then again 3 weeks later. He reports no wet nights after 1 month of combination therapy, then wets his bed once over the next 2 months. We continue to see him every 3 to 4 weeks and check his electrolytes every 2 to 3 months. He reports no side effects

Five months after starting combination therapy, Jimmy seems much more confident. He has gone 2 months without a bedwetting accident, and his face lights up while discussing the fun he had last week in summer camp. He remains free of side effects, and his parents are thrilled with his progress.

continued

Related resources

- National Association For Continence. www.nafc.org.
- Mayo ME, Burns MW. Urodynamic studies in children who wet. *Br J Urol* 1990 65;641-5.

DRUG BRAND NAMES

Desmopressin • DDAVP
Imipramine • Tofranil
Oxybutynin • Ditropan

DISCLOSURE

Dr. Williams is a speaker for Wyeth.

Dr. Singh reports no financial relationship with any company whose products are mentioned in this article, or with manufacturers of competing products.

We see Jimmy three more times, once every 2 months. He is staying "dry" but says he wishes to stop his medication because he wants to control his bladder without it.

When would you stop Jimmy's medication?
a) after he's accident-free for 1 year
b) after 6 months without an accident
c) after 3 months without an accident

The authors' observations

Medications and behavioral treatments can preserve the child's self-esteem until he or she outgrows enuresis (*Table, page 70*).

No guidelines address drug regimen duration. Tapering Jimmy's medications after 7 to 8 months seemed reasonable, but children with enuresis often relapse after stopping treatment. Researchers have recorded relapse rates as high as 60% after stopping imipramine and 80% after stopping desmopressin.[1,4]

Taper medications slowly to avoid withdrawal, immediate relapse, and anticholinergic effects. If the child relapses, restart medication at the previous therapeutic dosage(s), then start tapering after the child has been accident-free for 3 months.

Assess enuresis' psychological impact on the child; treat aggressively if social, emotional, or academic function is impaired. Urinary control medications can preserve the child's self-esteem by reducing or halting bedwetting until he or she outgrows the problem.

Bottom Line

FOLLOW-UP STILL DRY

After discussing the relapse risk with Jimmy's parents, we withdraw both oxybutynin and desmopressin over 2 months, reducing each dosage 25% every 2 weeks. We see Jimmy every 4 to 6 weeks during the taper period, then for two bimonthly follow-up visits. He reports no adverse effects and has been accident-free for 8 months.

After consulting with his pediatrician and family, we refer Jimmy, now age 13, back to the pediatrician. We have not seen him for more than 1 year.

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