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Yilmaz S, Bigic A, Herguner S. Effect of OROS methylphenidate on encopresis in children with attentiondeficit/hyperactivity disorder. J Child Adolesc Psychopharmacol. 2013; Oct 29. [Epub ahead of print]. 31.10b Enuresis EPIDEMIOLOGY The prevalence of enuresis ranges from 5 to 10 percent in 5-year-olds, 1.5 to 5 percent in 9- to 10-year-olds, and about 1 percent in adolescents 15 years and older. The prevalence of enuresis decreases with increasing age. Enuretic behavior is considered developmentally appropriate among young toddlers, precluding diagnoses of enuresis; however, enuretic behavior occurs in 82 percent of 2-year-olds, 49 percent of 3-yearolds, and 26 percent of 4-year-olds on a regular basis. In the epidemiological Isle of Wight study, investigators reported that 15.2 percent of 7-year-old boys were enuretic occasionally and that 6.7 percent of them were enuretic at least once a week. The study reported that 3.3 percent of girls at the age of 7 years were enuretic at least once a week. By age 10, the overall prevalence of enuresis was reported to be 3 percent. The rate drops drastically for teenagers: a prevalence of 1.5 percent has been reported for 14-year-olds. Enuresis affects about 1% of adults. Although most children with enuresis do not have a comorbid psychiatric disorder, children with enuresis are at higher risk for the development of another psychiatric disorder. Nocturnal enuresis is about 50 percent more common in boys and accounts for about 80 percent of children with enuresis. Diurnal enuresis is also seen more often in boys who often delay voiding until it is too late. A spontaneous resolution of nocturnal enuresis is about 15 percent per year. Nocturnal enuresis consists of a normal volume of voided urine, whereas when small volumes of urine are voided at night, other medical causes may be present. ETIOLOGY Enuresis involves complex neurobiological systems that include contributions from cerebral and spinal cord centers, motor and sensory functions, and autonomic and voluntary nervous systems. Urination is regulated by neurons in the pons and midbrain regions. Bladder detrusor muscle contraction occurs whenever bladder capacity is reached, which can lead to enuresis in a sleeping child. Therefore, excessive volumes of urine produced at night may lead to enuresis at night in children without any physiologic abnormalities. Nighttime enuresis often occurs in the absence of a specific neurogenic cause. Daytime enuresis may develop based on behavioral habits developed over time. Daytime enuresis may occur in the absence of neurological abnormalities resulting from habitual, voluntary tightening of the external sphincter during urges to urinate. The pattern may be set in a young child who may start out with a normal or overactive

detrusor muscle in the bladder, but with repeated attempts to prevent leaking or urination when there is an urge to void. Over time, the sensation of the urge to urinate is diminished and the bladder does not empty regularly, leading to enuresis at night when the bladder is relaxed and can empty without resistance. This immature pattern of urinating can account for some cases of

enuresis, especially when the pattern has been in place since early childhood. Most children are not enuretic by intention or even with awareness until after they are wet. Physiological factors often play a role in the development of enuresis, and behavioral patterns are likely to maintain the maladaptive urination. Normal bladder control, which is acquired gradually, is influenced by neuromuscular and cognitive development, socioemotional factors, toilet training, and genetic factors. Difficulties in one or more of these areas can delay urinary continence. Genetic factors are believed to play a role in the expression of enuresis, given that the emergence of enuresis has been found to be significantly greater in first-degree relatives. A longitudinal study of child development found that children with enuresis were about twice as likely to have concomitant developmental delays as those who did not have enuresis. About 75 percent of children with enuresis have a first-degree relative who has or has had enuresis. A child's risk for enuresis has been found to be more than seven times greater if the father was enuretic. The concordance rate is higher in monozygotic twins than in dizygotic twins. A strong genetic component is suggested, and much can be accounted for by tolerance for enuresis in some families and by other psychosocial factors. Studies indicate that children with enuresis with a normal anatomical bladder capacity report urge to void with less urine in the bladder than children without enuresis. Other studies report that nocturnal enuresis occurs when the bladder is full because of lower than expected levels of nighttime antidiuretic hormone. This could lead to a higher-than-usual urine output. Enuresis does not appear to be related to a specific stage of sleep or time of night; rather, bed-wetting appears randomly. In most cases, the quality of sleep is normal. Little evidence indicates that children with enuresis sleep more soundly than other children. Psychosocial stressors appear to precipitate enuresis in a subgroup of children with the disorder. In young children, the disorder has been particularly associated with the birth of a sibling, hospitalization between the ages of 2 and 4 years, the start of school, separation of a family due to divorce, or a move to a new environment. DIAGNOSIS AND CLINICAL FEATURES Enuresis is the repeated voiding of urine into a child's clothes or bed; the voiding may be involuntary or intentional. For the diagnosis to be made, a child must exhibit a developmental or chronological age of at least 5 years. According to DSM-5, the behavior must occur twice weekly for a period of at least 3 months or must cause distress and impairment in functioning to meet the diagnostic criteria. Enuresis is diagnosed only if the behavior is not caused by a medical condition. Children with

enuresis are at higher risk for ADHD compared with the general population. They are also more likely to have comorbid encopresis. DSM-5 and the 10th revision of International Statistical Classification of Diseases and Related Health Problems (ICD-10) break down the disorder into three types: nocturnal only, diurnal only, and nocturnal and diurnal. PATHOLOGY AND LABORATORY EXAMINATION No single laboratory finding is pathognomonic of enuresis; but clinicians must rule out organic factors, such as the presence of urinary tract infections, which may predispose a child to enuresis. Structural obstructive abnormalities may be present in up to 3 percent of children with apparent enuresis. Sophisticated radiographic studies are usually deferred in simple cases of enuresis with no signs of repeated infections or other medical problems. DIFFERENTIAL DIAGNOSIS To make the diagnosis of enuresis, organic causes of bladder dysfunction must be investigated and ruled out. Organic syndromes, such as urinary tract infections, obstructions, or anatomical conditions are found most often in children who experience both nocturnal and diurnal enuresis combined with urinary frequency and urgency. The organic features include genitourinary pathology—structural, neurological, and infectious—such as obstructive uropathy, spina bifida occulta, and cystitis; other organic disorders that can cause polyuria and enuresis, such as diabetes

mellitus and diabetes insipidus; disturbances of consciousness and sleep, such as seizures, intoxication, and sleepwalking disorder, during which a child urinates; and adverse effects from treatment with antipsychotic agents. COURSE AND PROGNOSIS Enuresis is often self-limited, and a child with enuresis may have a spontaneous remission. Most children who master the task of control over their bladder gain selfesteem and improved social confidence when they become continent. About 80 percent of affected children have never achieved a year-long period of dryness. Enuresis after at least one dry year usually begins between the ages of 5 and 8 years; if it occurs much later, especially during adulthood, organic causes must be investigated. Some evidence indicates that late onset of enuresis in children is more frequently associated with a concomitant psychiatric difficulty than is enuresis without at least one dry year. Relapses occur in children with enuresis who are becoming dry spontaneously and in those who are being treated. The significant emotional and social difficulties of these children usually include poor self-image, decreased self-esteem, social embarrassment and restriction, and intrafamilial conflict. The course of children with enuresis may be influenced by whether they receive appropriate evaluation and treatment for common comorbid disorders such as ADHD.

TREATMENT A relatively high rate of spontaneous remission of enuresis occurs over time in childhood; however, in many cases, interventions are necessary because enuresis is causing functional impairment. The first step in any treatment plan is to review appropriate toilet training. If toilet training was not attempted, the parents and the patient should be guided in this undertaking. Record-keeping is helpful in determining a baseline and following the child’s progress, and may itself be a reinforcer. A star chart may be particularly helpful. Other useful techniques include restricting fluids before bed and night lifting to toilet train the child. Interventions with alarm therapy, which is triggered by wet underwear, has been a mainstay of treatment for enuresis. Alarm therapy works by alerting a child to respond when voiding begins during sleep. The alarm is a battery-operated device that can be attached to a child’s underwear or a mat. The alarm is triggered as soon as voiding begins by emitting a loud noise that awakens the child. The success of this method is based on the child’s ability to awaken promptly and respond to the alarm by getting up and voiding in the toilet. A child who can respond optimally is at least 6 or 7 years old. Pharmacological interventions including desmopressin therapy in managing nocturnal enuresis have been shown to be effective in some patients. Desmopressin is a “synthetic analogue” of vasopressin, which can be administered as a pill, a sublingual melt, or a nasal spray. Its effect can last up to 8 hours, and it works by reducing urine production at night. This method is optimal when no fluids are ingested in the evening. Another basic intervention for those children with enuresis and bowel dysfunction is to assess whether chronic constipation is contributing to urinary dysfunction, and to consider increasing dietary fiber to diminish constipation. Behavioral Therapy Classic conditioning with the bell (or buzzer) and pad (alarm) apparatus is generally the most effective treatment for enuresis, with dryness resulting in more than 50 percent of cases. Bladder training—encouragement or reward for delaying micturition for increasing times during waking hours—has also been used. Although sometimes effective, this method is decidedly inferior to the bell and pad. Pharmacotherapy Medication is considered when enuresis is causing impairment in social, family, and school function and behavioral, dietary, and fluid restriction have not been efficacious. When the problem interferes significantly with a child’s functioning, several medications can be considered, although the problem often recurs as soon as medications are withdrawn. Desmopressin (DDAVP), an antidiuretic compound that is available as an intranasal spray, has shown success in reducing enuresis. Reduction of enuresis has varied from 10 to 90

percent with the use of desmopressin. In most studies, enuresis recurred shortly

after discontinuation of this medication. Adverse effects that can occur with desmopressin include headache, nasal congestion, epistaxis, and stomachache. The most serious adverse effect reported with the use of desmopressin to treat enuresis was a hyponatremic seizure experienced by a child. Reboxetine (Edronax, Vestra), a norepinephrine reuptake inhibitor with a noncardiotoxic side effect profile has recently been investigated as a safer alternative to imipramine in the treatment of childhood enuresis. A trial in which 22 children with enuresis causing social impairment, who had not responded to an enuresis alarm, desmopressin, or anticholinergics were administered 4 to 8 mg of reboxetine at bedtime. Of the 22 children, 13 (59 percent) in this open trial achieved complete dryness with reboxetine alone, or in combination with desmopressin. Side effects were minimal and did not lead to discontinuation of the medication in this trial. Psychotherapy Psychotherapy may be useful in dealing with the coexisting psychiatric problems and the emotional and family difficulties that arise secondary to chronic enuresis. REFERENCES Baeyens D, Roeyers H, D'Haese L, Pieters F, Hoebeke P, Vande Walle J. The prevalence of ADHD in children with enuresis: Comparison between a tertiary and non-tertiary care sample. Acta Paediatr. 2006;95:347. Brown ML, Pope AW, Brown EJ. Treatment of primary nocturnal enuresis in children: A review. Child Care Health Dev. 2010;37:153–160. Butler RJ, Heron J. The prevalence of infrequent bedwetting and nocturnal enuresis in childhood: A large British cohort. Scand J Urol Nephrol. 2008;42:257–264. Feldman AS, Bauer SB. Diagnosis and management of dysfunctional voiding. Curr Opin Pediatr. 2006;18:139. Fitzgerald MP, Thom DH, Wassel-Fyr C, Subak L, Brubaker L, Van Den Deden SK, Brown JS. Childhood urinary symptoms predict adult overactive bladder symptoms. J Urol. 2006;175:989. Friedman FM, Weiss JP. Desmopressin in the treatment of nocturia: clinical evidence and experience. Ther Adv Urol. 2013;5:310–317. Kajiwara M, Inoue K, Kato M, Usui A, Kurihara M, Usui T. Nocturnal enuresis and overactive bladder in children: An epidemiological study. Int J Urol. 2006;13:36. Klages T, Geller B, Tillman R, Bolhofner K, Zimerman B. Controlled study of encopresis and enuresis in children with a prepubertal and early adolescent bipolar-I disorder phenotype. J Am Acad Child Adolesc Psychiatry. 2005;44:1050. Landgraf JM, Abidari J, Cilento BG Jr., Cooper CS, Schulman SL, Ortenberg J. Coping, commitment, and attitude: Quantifying the everyday burden of enuresis on children and their families. Pediatrics. 2004;113:334. Mikkelsen EJ. Elimination disorders. In: Sadock BJ, Sadock VA, Ruiz P, eds. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th ed. Vol. II. Philadelphia: Lippincott Williams & Wilkins; 2009:3624. Nevus T. Reboxetine in therapy-resistant enuresis: results and pathogenetic implications. Scand J Urol Nephrol. 2006;40:31. Pennesi M, Pitter M, Borduga A, Minisini S, Peratoner L. Behavioral therapy for primary nocturnal enuresis. J Urol. 2004; 171:408. Perrin N, Sayer L, White A. The efficacy of alarm therapy versus desmopressin therapy in the treatment of primary mono-

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