NOCTURNAL ENURESIS

Method of
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CURRENT DIAGNOSIS

- Nocturnal enuresis is defined as involuntary nighttime bedwetting in a child at least 5 years of age.
- Primary nocturnal enuresis is present when the child has never achieved a period of nighttime dryness greater than 6 consecutive months. Secondary nocturnal enuresis is present when the child has experienced a period of nighttime dryness of at least 6 consecutive months.
- The most common causes of primary nocturnal enuresis are a deep sleep pattern, nocturnal polyuria, and a small-capacity bladder or nocturnal detrusor overactivity.
- A urinalysis is warranted to rule out urinary tract infection, glycosuria, and a defect in the ability to concentrate urine.
- Ultrasound examination of the bladder (prevoid and postvoid) can be used to evaluate bladder dysfunction and functional bladder capacity.

CURRENT THERAPY

- Desmopressin (DDAVP, 1-deamino-8-arginine vasopressin) is indicated as a first-line therapy for children with monosymptomatic nocturnal enuresis associated with nocturnal polyuria and normal bladder function.
- Enuretic alarm is indicated as a first-line therapy for children with monosymptomatic nocturnal enuresis associated with a small bladder capacity or in children with severe enuretic symptoms refractory to desmopressin therapy.
- Behavioral therapy such as encouraging the child to urinate frequently during the daytime, emptying the bladder before bedtime, and restricting fluid in the evening may increase the success rate of pharmacologic therapy or enuretic alarm therapy.

Nocturnal enuresis is defined as involuntary nighttime bedwetting in a child at least 5 years of age. Primary nocturnal enuresis is present when the child has never achieved a period of nighttime dryness greater than 6 consecutive months. Secondary nocturnal enuresis is present when the child has experienced a period of nighttime dryness of at least 6 consecutive months. For the majority of children with secondary nocturnal enuresis, the pathogenesis is no different from that of primary nocturnal enuresis.

Nocturnal enuresis is a common problem that is frustrating for children, parents, and physicians alike. The condition may affect the child's self-esteem and may lead to reduced social interaction and behavioral problems.

Epidemiology

It has been estimated that 15% to 25% of 5-year-old children and 5% to 10% of 7-year-old children have nocturnal enuresis. Without specific treatment, approximately 15% of affected children become dry each year. The male-to-female ratio is approximately 3:1.

Risk Factors

Encopresis, daytime wetting (diurnal enuresis), and male gender are significant risk factors. Constipation, emotional stress, developmental delay, bladder dysfunction, sleep deprivation, adenotonsillar hypertrophy, and attention-deficit/hyperactivity disorder also play a role.

Pathogenesis

The most common causes of primary nocturnal enuresis are a high arousal threshold, nocturnal polyuria, and a small-capacity bladder or nocturnal detrusor overactivity. Although these causes may overlap, it is important to conceptualize them separately, because this differentiation will help the physician to understand the problem, to educate both the parents and child, and to plan an appropriate treatment program.

It has been shown that enuretic children have a high arousal threshold and a reduced prepulse inhibition of startle. In most children, arousability from sleep improves with maturation of the central nervous system.

In most circumstances, the rate of secretion of antidiuretic hormone from the posterior pituitary gland is increased at night. This circadian variation is usually established when the child is 3 to 4 years old. Some children with primary nocturnal enuresis have a lack of this circadian variation with an abnormally low nocturnal secretion of antidiuretic hormone with resultant nocturnal polyuria. Other causes of nocturnal polyuria include fluid and solute overload in the evening.

Children with a small-capacity bladder or nocturnal detrusor overactivity often have primary nocturnal enuresis. Conditions that may reduce the functional bladder capacity include cystitis and constipation.

There is a strong genetic component to nocturnal enuresis. The child of parents who were both enuretic has a 77% chance of developing enuresis. If one parent was enuretic, there is up to a 44% occurrence rate. If neither parent was enuretic, the occurrence rate is only 15%. Twin studies also support a genetic basis for nocturnal enuresis: the concordance rate is much higher in monozygotic twins (68%) when compared with dizygotic twins (36%). Linkage studies have suggested possible genetic markers for primary nocturnal enuresis located on chromosomes 12, 13, and 22.

A neurogenic bladder is one of the few anatomic abnormalities that can cause primary nocturnal enuresis. Congenital urethral obstruction is another infrequent anatomic cause of primary nocturnal enuresis. The enuresis in these children is due to an overflow phenomenon from a poorly compliant bladder. The most common cause of urethral obstruction in the male is posterior urethral valves. Girls and boys with significant congenital urethral stenosis may also present with this problem. An ectopic ureter or vesicovaginal fistula is an infrequent anatomic cause of primary nocturnal enuresis in girls.

A defect in the ability of the kidney to concentrate urine can cause primary nocturnal enuresis. The causes of concentrating defects include any cause of chronic renal failure and diabetes insipidus.

Diagnosis

History

Onset and Frequency

The timing of the onset and the frequency of nocturnal enuresis are important historical clues to the etiology. Secondary nocturnal enuresis and intermittent nocturnal enuresis are not usually associated with structural abnormalities in the urinary tract. Nocturnal enuresis due to a structural abnormality of the urinary tract is usually present from birth and is not associated with periods of remission.

Timing, Frequency, and Volume per Episode

A history of soaking absorbent underpants in the morning suggests nocturnal polyuria. Parents of children with nocturnal polyuria often remark that the volume of urine associated with the enuretic episode or the first morning void is very large. Frequent episodes of nocturnal enuresis with a small volume of urine suggest bladder dysfunction such as may occur with a urethral obstruction or a neurogenic bladder. Several episodes of nocturnal enuresis with a large volume suggest diabetes mellitus or

diabetes insipidus. Constant wetting suggests an ectopic ureter or vesicovaginal fistula.

Associated Symptoms

Nocturnal enuresis associated with daytime urinary frequency, urgency, incontinence, and difficulties in initiating the urinary stream suggests urethral obstruction. Daytime urinary frequency, urgency, incontinence, squatting behavior, constipation, encopresis, gait disturbance, and a history of spina bifida or spinal trauma suggest a neurogenic bladder. Constant dampness in the underwear by day and night in a female suggests an ectopic ureter or vesicovaginal fistula. Secondary nocturnal enuresis associated with dysuria, urinary frequency, urgency, fever, suprapubic/loin pain, or cloudy, foul-smelling urine suggests a urinary tract infection. Polyuria, polydipsia, polyphagia, and weight loss suggest diabetes mellitus. Polyuria, polydipsia, and episodes of dehydration in a child with a history of central nervous system disease suggest diabetes insipidus. A history of constipation is important because the condition is associated with a reduced functional bladder capacity.

Volume of First Morning Void

Most children with nocturnal enuresis void only a small or average amount of urine in the morning after an enuretic episode. A large volume of urine voided following a significant episode of nocturnal enuresis may be a clue to the presence of low nocturnal secretion of antidiuretic hormone.

Soundness of Sleep

Children with nocturnal enuresis often sleep more deeply than other family members. Some children only wet when they are overtired. Conversely, children who are usually enuretic may be continent during periods of wakeful sleep such as during intercurrent illnesses.

Past Health

A child with a history of a structural abnormality of the urinary tract or neurogenic bladder may have nocturnal enuresis due to these causes. A history of spinal trauma may indicate a neurogenic bladder as a cause of enuresis. A history of central nervous system disorder may indicate neurogenic diabetes insipidus. Certain medications such as methylxanthines and caffeine may be associated with nocturnal enuresis.

Family History

A family history of nocturnal enuresis should be sought because nocturnal enuresis tends to run in the family. A family history of diabetes mellitus, diabetes insipidus, or kidney disease suggests the corresponding disorder. Any stressful events in the family such as birth of a sibling and parental disharmony should be explored, especially in children with secondary nocturnal enuresis.

Physical Examination

Height and weight should be measured and plotted onto standard growth charts. All children should have their blood pressure checked, which, if elevated, might indicate renal disease. A thorough physical examination should include examination of the abdomen and genitalia and a complete neurologic examination. In chronic constipation, fecal masses are often palpable in the left lower quadrant of the abdomen and in the suprapubic area.

In the majority of children with primary nocturnal enuresis, the physical examination is unremarkable. An abnormal physical examination is only present when primary nocturnal enuresis is due to a structural cause. A myelomeningocele is usually obvious at birth; however, subtle spinal defects may also be associated with primary nocturnal enuresis. A midline tuft of hair, an exaggerated dimple, or a birthmark in the area of the lumbosacral spine; a gait abnormality; absence of anal wink; or abnormal motor power, tone, reflexes, or sensation in the lower extremities suggests a neurogenic bladder. A palpably enlarged bladder or kidney and a weak or dribbling urinary stream suggests urinary obstruction, such as may result from posterior urethral valves.

Laboratory and Imaging Studies

A urinalysis is warranted to rule out urinary tract infection, diabetes mellitus, and a defect in the ability to concentrate urine. Ultrasound examination of the bladder (prevoid and postvoid) can be used to evaluate bladder dysfunction and functional bladder capacity.

Treatment

One essential part of the treatment plan of every child with primary nocturnal enuresis should be compassion and support from both the family and physician. It is important to clarify to parents that the child is not at fault and to specify that punishment for bedwetting is inappropriate. The child and family can be reassured that in the absence of structural defect, primary nocturnal enuresis tends to resolve with time.

Simple behavioral strategies such as encouraging the child to urinate frequently during the daytime, emptying the bladder before bedtime, and limiting fluid and solute intake in the evening are often recommended. Caffeinated beverages should be avoided, particularly in the evening. Some authors recommend waking the child 1.5 to 2 hours after bedtime to go to the bathroom. Star charts and reward systems need to reinforce positive behavior. Behavioral therapy may increase the success rate of pharmacologic therapy or enuretic alarm therapy.

Desmopressin (DDAVP, 1-deamino-8-arginine vasopressin) is an analogue of vasopressin that has a profound antidiuretic activity without pressor activity. The medication acts on the V2 receptors of the renal tubules and increases the reabsorption of fluid from the renal tubules, thereby decreasing the amount of urine produced. The medication is indicated as a first-line therapy for children with monosymptomatic nocturnal enuresis associated with nocturnal polyuria and normal bladder function. Desmopressin is available in a sublingual lyophilisate (melt) preparation,[2] as well as a tablet. The bioavailability of the lyophilisate (melt) preparation is approximately 60% greater than that of the tablet formulation. The recommended dose of desmopressin is 120 to 240 μg melt and 200 to 400 μg tablet. The former is usually given 30 minutes to 1 hour before bedtime, and the latter is usually given 1 hour before bedtime. Side effects are rare and include symptomatic hyponatremia with water intoxication. When desmopressin is prescribed, patients should be instructed to avoid high fluid intake in the evening.

Imipramine (Tofranil), a tricyclic agent with antimuscarinic property, may be helpful in children who have not responded to desmopressin alone. Presumably, the medication decreases the amount of time spent in rapid eye movement sleep, stimulates antidiuretic hormone secretion, and relaxes the detrusor muscle. The recommended starting dose is 25 mg for children 6 to 12 years of age and 50 mg for those older than 12 years, given 1 to 2 hours before bedtime. If necessary, the dose may be increased gradually to a maximum of 50 mg in children 6 to 12 years of age and 75 mg for those older than 12 years. However, potential side effects (anxiety, depression, dizziness, headache, drowsiness, lethargy, sleep disturbance, dry mouth, anorexia, vomiting, skin rashes) and serious adverse effects (hepatotoxicity, cardiotoxicity) with overdose limit their use.

Monotherapy with oxybutynin (Ditropan),[1] an anticholinergic and antispasmodic agent that decreases uninhibited bladder contraction, is not effective in treating monosymptomatic nocturnal enuresis. The medication can be added, however, as a second-line drug in the treatment of children with both diurnal and nocturnal enuresis. The dose is 5 mg administered 1 hour before bedtime.

Enuretic alarm is indicated as a first-line therapy for children with monosymptomatic nocturnal enuresis associated with a small bladder capacity or nocturnal detrusor overactivity.

[1] Not FDA approved for this indication.
[2] Not available in the United States.

Randomized controlled trials have demonstrated that the enuretic alarm has greater efficacy than other forms of treatment. The enuretic alarm is triggered when a sensor in the sheets or night clothes gets wet; a bell or buzzer is thereby activated. Presumably, alarm therapy startles the child and improves arousal from sleep either by classical conditioning or avoidance conditioning. A disadvantage of alarm therapy is that it takes a couple of weeks to take effect. As such, alarms should be used for at least 6 weeks in children who do not respond before discontinuing their use. Because success depends on a cooperative, motivated child, conditioning therapy with an alarm device is generally used in children over 6 years of age.

It has been shown that combination of alarm and desmopressin works better than either treatment alone. Such treatment may be considered for children with refractory nocturnal enuresis.

When an anatomic abnormality or defect in urinary concentration ability is present, the underlying problem may require specific dietary, pharmacologic, or surgical treatment. Any underlying constipation should also be treated.

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INFANT AND CHILDREN FEEDING PROBLEMS

Method of

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CURRENT DIAGNOSIS

- As of 2021, the primary diagnostic code used to describe feeding problems in infants and children is *pediatric feeding disorder (PFD).*
- PFD is defined as impairments in oral intake that are not age appropriate.
- PFD is caused by medical, nutritional, psychosocial, and/or feeding skill problems.
- As a result of both the broad criteria and the complex multifactorial nature of the condition, the presentation of PFD can vary significantly from child to child, as can treatments.

CURRENT THERAPY

- A thorough assessment of medical, nutritional, psychosocial, and feeding skills issues is needed to optimize treatment planning.
- It is imperative to treat underlying medical conditions that may be contributing to pediatric feeding disorder.
- Nutritional monitoring is necessary to ensure patient safety and guide clinical decision-making.
- If adequate nutrition cannot be achieved orally, enteral nutrition should be considered.
- Feeding therapy is often necessary to treat feeding skill issues that prevent safe or efficient oral feeding.
- Behavioral treatment is often needed to treat parent and/or child factors that prevent oral feeding.

Pathophysiology

As of 2021, pediatric feeding disorder (PFD) is the primary diagnosis used to describe feeding problems of infants and children. PFD is often multifactorial, including medical, nutritional, psychosocial, and skill-based issues, and typically involves concerns in one or more of these domains. The progression of feeding from breastmilk or formula at birth to table foods is a typical pattern of development that occurs without issue for many children. However, when this typical pattern of development is interrupted, PFD can develop.

Medical etiologies: Cow's milk protein allergy, gastroesophageal reflux disease, and eosinophilic esophagitis are the most common gastrointestinal (GI) etiologies of PFD. They can lead to discomfort with feeding that can contribute to the development of a feeding aversion. Although less common, physiologic processes that increase metabolic demand can lead to PFD, as they make it difficult for the infant or child to keep up with their caloric needs. This is most common in children with congenital heart disease. Medical conditions, such as cardiorespiratory compromise during oral feeding and aspiration and recurrent aspiration pneumonitis, may be causes of feeding problems. Underlying syndromes, neuromuscular disabilities, and genetic differences can interrupt the typical progression of feeding, contributing to feeding intolerance, poor oral intake, or oral aversion. Premature infants who spent time in the neonatal intensive care unit have an increased incidence of feeding difficulties that can be, in part, due to delay of development and multiple painful procedures around their mouth and face that can contribute to oral aversion.

Nutritional etiologies: A nutritional deficit may result from inadequate caloric intake, increased metabolic demand, or excessive GI losses. Inadequate caloric intake can be caused by a decreased hunger drive, often from a grazing pattern of eating, which effectively alleviates the child's sensation of hunger. Therefore the child does not eat an adequately sized meal. Increased metabolic demand results from a medical condition that causes the patient to be unable to gain weight even with usually adequate caloric intake as their nutritional needs are greater than typical for age. This can include such etiologies as congenital heart disease, cystic fibrosis, metabolic disorders, or neuromuscular disorders. Excessive GI losses may occur with vomiting or diarrhea, where calories that are taken in are not effectively used. Malnutrition and nutrient deficiencies may result from a lack of dietary diversity.

Psychosocial etiologies: Infants and children can develop aversions to feeding for several reasons. Psychosocial etiologies may interact with medical or feeding skill concerns. For instance, a child may begin refusing all foods because of a cow's milk allergy