1. Introduction

Nocturnal enuresis is a much more common disorder than perceived from the perspective of Primary Care. It becomes less prevalent with age and tends to resolve spontaneously, albeit not in all cases or necessarily at the desired time. Oftentimes it resolves too late, having a negative emotional impact on the child, generating extra expense and work for the parents, and even problems in the child's social relationships.

In recent decades the start of sphincter control training tends to take place later[1]. However, the demands of our western culture mean that children often sleep away from home (friends' houses, camps…) at ever earlier ages, and bedwetting is a problem for both parents and children.

If we, from Primary Care, were able to contribute to early resolution, prevention of complications, and identification of cases with a poor course of the condition, we would solve most of the problems created by nocturnal enuresis. However, in order to do so, we need to gain in-depth knowledge about the subject, its magnitude, and how approach it efficiently.

Most of the epidemiological data available come from cross-sectional studies based on parent surveys. Said data clearly reveal that inheritance plays a key role in nocturnal enuresis. The most common means of transmission is autosomal dominant with high penetrance (90%), although in one-third of the cases it presents sporadically[2]. In an Italian study[3], the risk of having nocturnal enuresis was 6 times greater when there was a positive parental history (OR 6.7; 95% CI: 4.4-10.4). In another cross-sectional study, the risk of enuresis was 5-7 times higher when only one of the parents had a positive history of enuresis, rising to 11.3 times if both parents had a history of the disorder[4]. Molecular genetics links enuresis to alterations in chromosomes 8, 12, 13 and 22[5,6].

Generally speaking, prevalence studies cover all kinds of enuresis without distinguishing between primary, secondary, monosymptomatic, and non-monosymptomatic enuresis. Another major problem is the use of different con-

Table VI. *Prevalence of enuresis in different countries*

Author	Year	Origin	Definition	N	Age	Prevalence
Marugan[7]	1996	Spain	> 1 incident/month	1307	6 y 10 y	13.09% 7.49%
Roquer[8]	1999	Spain	> 2 incidents/month	720	5-14 y 5 y 6 y 7-10 y 11-14 y	8.3% 12% 11.8% 9% 1%
Chiozza[3]	1998	Italy	NE DSM III and DSM IV	6.892	6-14 y	DSM III: 3.8% DSM IV: 1.7%
Spee-Van Der Wekke[9]	1998	Netherlands	Primary and secondary NE	7.931	5-15 y 5-6 y 13-15 y	6% 15% 1%
Bakker[10]	2002	Belgium	Monosymptomatic NE	4.332	10-14 y	1%
Lottman[11]	1999	France	Primary and secondary NE	3.803	5-10 y 5-7 y	9.2% 11.2%
Gümüs[12]	1999	Turkey	2 incidents/week	1.703	7-11 y	13.7%
Serel[13]	1997	Turkey	Primary and secondary NE	5.523	7-12 y	11.5%
Kalo[14]	1996	Saudi Arabia	Primary and secondary NE	740	6-16 y	13%
Ouedraogo[15]	1997	Burkina Faso	Primary and secondary NE	1.575	5-16 y	12.95% PMNE: 10.2%
Chang[16]	2001	Taiwan	Primary NE	1.176	6-11 y	8%
Lee[17]	2000	Korea	> 1 incident/month	7.014	7-12 y	9.2%
Liu[18]	2000	China	>1 incident/3 months	3.334	6-16 y	4.3%
Kanaheswari[19]	2003	Malaysia	Primary NE	2.487	7-12 y 7 y 9 y 12 y	NE: 8% PNE: 6.2% 9% 7.6% 1-2%
Bower[20]	1996	Australia	1 incident/month	2.292	5-12 y	15%
Byrd[21]	1996	USA	Primary and secondary NE	10.960	5 y 8 y 11 y 18 y	33% 18% 7% 0.7%

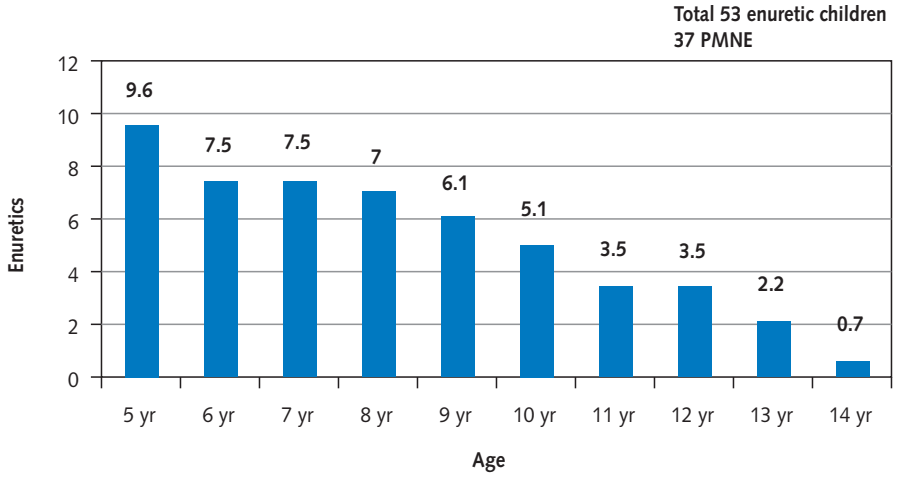
NE: nocturnal enuresis; PNE: primary nocturnal enuresis; y: years old.

ceptual definitions, including that of enuresis itself, which sometimes makes it difficult to compare results. An example of this can be seen in the study by Chiozza et al[3], in which the prevalence of enuresis in a single population varies from 3.8% to 1.7% depending on the definition used, DSM III or DSM IV (table VI).

Despite all these problems, the prevalence of enuresis worldwide is estimated at 16% at 5 years of age and 1-3 % in adolescents and adults, with a higher incidence in males (1.5/1). Data on the Spanish child population show a similar prevalence to that described in other European countries[7,8]. Lower prevalence has been found in studies from Asian countries (table VI).

Based on prevalence figures for enuresis by age and extrapolating the data to the Spanish population according to the 2001 census, we can estimate that for the 1000 pediatric patients allocated per pediatrician, probably 53 children aged 5 to 14 years suffer nocturnal enuresis. If we also bear in mind that primary nocturnal enuresis represents 80% of all cases and PMNE (primary monosymptomatic nocturnal enuresis), the 85% of the last group[22], of the 1000 children, 37 would have this type of enuresis, a figure which is not negligible (figure 1).

Figure 1. *Prevalence of primary monosymptomatic nocturnal enuresis in a Primary Care pediatrician's office. 2001 census Data for a clinic caring 1000 patients.*



Primary Care perceives a much lower prevalence of the disorder, due to the fact that most of these children have not been diagnosed, either because of parental tolerance, many of whom had also had the same problem, or because they do not consider it important, or hide it because they feel ashamed, and oftentimes, too, because of the tolerance of the pediatrician him/herself.

In order to approach the diagnosis and treatment of a child with enuresis, the parents' and the child's awareness of the problem and their seeking help are as important as the pediatrician's being motivated and being knowledgeable enough about the disorder.

In a Spanish survey of parents, the majority responded that the pediatrician is the professional who should treat the bedwetting child. Although they consider that bedwetting is a problem for the child, a high percentage of parents believe that patience and playing down the problem are the best approach. 34% of the parents believe that diapers are a good remedy for this situation and even today, 14% feel that a child who wets the bed should be punished[23].

In another survey conducted among Spanish pediatricians, certain confusion is observed insofar as when treatment should be started is concerned, and a remarkably high percentage of them expect spontaneous remission to occur. When they decide to refer the child to specialist care, the most widely referred specialist is the psychologist, though the fact that pharmacotherapy is the most widely accepted treatment by these very same pediatricians, possibly because it is better known[24].

We need to acknowledge the fact that during pediatric training in hospitals, little attention is paid to enuresis, perhaps because it is not deemed to be a serious disorder, or because it tends to resolve spontaneously, obviating the psychosocial problems that it creates. This has meant that, though most of the cases could have been resolved at an early stage by Primary Care pediatricians, the problem is underestimated and left untreated, or the child is referred to other specialists, leaving 1-3% of these patients who reach adulthood as bedwetters.

Pathophysiology

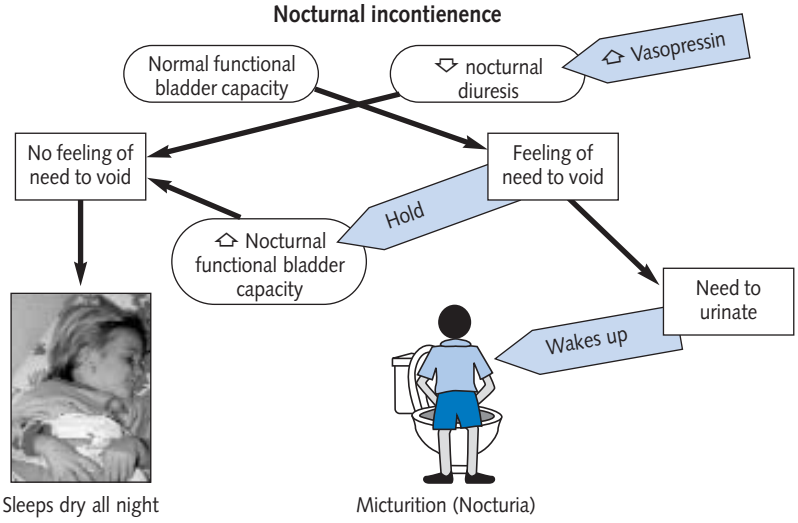
The sequence of the physiological phenomena of normal micturition during the day is well known. The filling phase is imperceptible, such that the bladder fills with urine without increasing pressure, adjusting to its content level. At a certain point in the filling phase, the desire to

void appears. At that time, the child can decide whether to withhold or void. If he/she decides to withhold, the bladder adjusts to the urine content and the desire to void may disappear. Later on, with a greater urinary volume, a greater and perhaps more urgent desire to void appears, which can no longer be fully repressed (or it can be repressed but for a shorter period of time), but urine can be withheld (even though the desire to void persists) for quite a while, until a socially appropriate time when the individual can void voluntarily.

At night the body makes use of a series of mechanisms to maintain continence that are different from daytime mechanisms (figure 2).

- Firstly, nocturnal diuresis is decreased: urine output by the kidneys does not remain uniform over 24 hours; rather, its rhythm is related to the circadian rhythm of vasopressin secretion, which increases at night in such a way that urinary output is less while sleeping than during the daytime. This in itself could avoid the need to void at night.
- Secondly, an increase in nocturnal bladder capacity: the urinary retention mechanism is heightened, so that the voided volume of the first morning void (after retention during sleep) is 1.6 to 2.1 times greater than the maximum voided volume of daytime voids[25].

Figure 2. *Physiology of nocturnal urinary continence.*

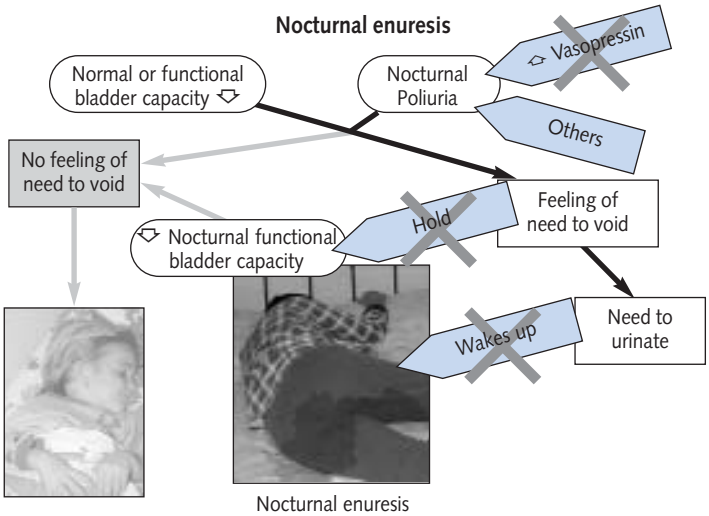


– - Thirdly, when the desire to void persists and is sufficiently intense, arousal takes place: the child wakes up and goes to the toilet (nocturia). There is an 11.2% rate of physiological nocturia[26].

Enuresis requires:

– Always:
  • Failure in arousal as a result of the desire to void, otherwise we would be referring to nocturia and not enuresis. The ability to arouse to a given stimulus is not the same all night long or even on different nights. It is not unusual to find children that only wet the bed when they are very tired or feel very sleepy (after 'special' days…), or get up at dawn, yet wet the bed in the early hours of the night. One reason for a failure in arousal can be the lack of the perception of the desire to void.
– In addition, at least one of the following circumstances:
  • Increased nocturnal urinary output.
  • Decreased nocturnal functional bladder capacity due to
    – nocturnal instability or
    – insufficiency of the urinary withholding mechanism.

Figure 3. *The pathophysiology of enuresis.*



The inability to wake up does not necessarily lead to enuresis. There are children without enuresis who are not able to wake up because of the desire to void, although they have good bladder capacity and/or a suitable decrease in nocturnal diuresis. They have developed nocturnal continence at the expense of a great ability to "withhold" that avoids the need to urinate at night. These children either withhold or wet the bed, they never wake up, and when diuresis is forced, for example with water loading (25 ml/kg), they are enuretic. These cases represent 31% of the normal pediatric population[27].

Nocturnal enuresis is the consequence of a mismatch between nocturnal urinary output and nocturnal bladder capacity and is always associated with the inability to arouse (figure 3).

Natural history

Longitudinal studies on the natural course of enuresis are no longer ethically possible, because many of the children affected receive treatment. Past studies showed annual remission rates of 15% at 5 to 9 years of age, 16% in children aged 10 to 14, and 16% in adolescents aged between 15 and 19 years, with 3% of enuretic patients being adult (over 20 years of age)[28].

The "1946 British birth cohort" (Medical Research Council 1946, National Survey of Health Development) included all children born in the week of 3-9 March 1946 to married couples in England, Scotland and Wales. This cohort initially consisted of 5362 children and was followed up on 20 occasions, most recently at the age of 53 (in 1999) and the first ten occasions before the participants reached 16 years of age, with a follow-up of 91% of the cohort during that period of childhood. It provides prospective data on enuretic children at 6 endpoints: 4, 6, 8, 9, 11 and 15 years of age (corresponding to the years 1950, 52, 54, 55, 57 and 61). At each age we know if the child wet the bed or not in the previous month (at least once); we also have data available on daytime wetting (never, "once or more"), the age at which the parents started toilet training (sphincter control), the age when diapers were withdrawn, the age at which the children controlled defecation, and the existence of subsequent problems with defecation control.

Croudace et al[29] have recently re-analyzed this cohort of 3272 children with complete data and 1483 with partially incomplete data (total= 4755; 90.9% of the cohort). Through a complex statistical methodology (latent class models for mi-

Table VII. *Developmental patterns of nocturnal continence*

Developmental pattern	% of the general population	% de los enuréticos	
Normal	84.0%		Nocturnal bladder control before 4-6 years of age
Transient enuresis	8.7%	54.37%	Remission between 6 and 8 years of age
Persistent enuresis	1.8%	11.25%	Persists until 8 years of age and gradually resolves by the time the patient is 15 years of age
Chronic bedwetting	2.6%	16.25%	Persists until 11 years of age. At 15, they continue to wet the bed, sometimes less than once a month
Relapsing enuresis	2.9%	18.13%	Children with late onset enuresis who recover and relapse until 15 years of age. Secondary enuresis

xed variables) they have been able to determine 5 models or "developmental trajectory classes" of nocturnal urinary continence: the normal one plus another 4 models or patterns of enuresis with very little overlap, in such a way that few children develop differently from these 5 models [Ib] (table VII).

There are no studies that make it possible to estimate the age at which one child in particular will stop wetting the bed.