

# Enuresis and spontaneous cure rate

## Study of 1129 enuretics

W. I. FORSYTHE and A. REDMOND

*From the Royal Belfast Hospital for Sick Children, Belfast*

**Forsythe, W. I., and Redmond, A. (1974).** *Archives of Disease in Childhood*, **49**, 259. **Enuresis and spontaneous cure rate: study of 1129 enuretics.** A long-term follow-up of 1129 children with nocturnal enuresis, not treated by the electric alarm, has shown that the annual spontaneous cure rate between 5 and 9 years of age was 14%, between 10 and 14 years 16%, and between 15 and 19 years 16%. 33 patients (3%) were still wetting after 20 years.

Organic cause for enuresis and the ineffectiveness of drug therapy are discussed.

In spite of numerous reports on the treatment of enuresis, it is surprising that there is little or no information regarding spontaneous cure rates at each year of age. In order to obtain this information we have followed up all those children who attended the Enuretic Clinic from 1952 to 1959 and who had not been treated by the electric alarm. Questionnaires were sent to 1483 parents and 1157 replies were received.

We define enuresis as an involuntary discharge of urine by a child of 5 years or more. It may be nocturnal, nocturnal and diurnal, or diurnal alone. Primary nocturnal enuresis refers to the child who has never been dry at night, and secondary or acquired nocturnal enuresis refers to the child who has been dry for at least a year before the onset of enuresis. 55 children with diurnal enuresis and 17 children with nocturnal enuresis cured by surgery and 11 cured by drug treatment, seen during the above period, have been excluded.

An enuretic clinic was started in 1952. At the beginning most patients were referred by general practitioners and hospital colleagues, but later approximately 75% of the patients were referred by doctors attached to the school medical service in Belfast as a result of their routine visits to the schools.

A detailed history was obtained from the mother in 97% of cases and from the father or relatives in the remainder. The first 800 patients were subjected to a detailed neurological examination in

the hope of finding an organic cause for the enuresis, but the results were so disappointing that the initial clinical examination was later confined to the abdomen, thoracolumbar area, and external genitalia, together with a rectal examination. A midstream specimen of urine was examined for pus cells and cultured for organisms. The act of micturition was observed when the midstream specimen of urine was obtained and during cystography, because little reliance could be placed on the mother's observation that her child 'dribbled' or 'stopped and started' during voiding. Parents rarely observe their children voiding, and most assume that the child dribbles if the pants are wet. A blood sample for urea estimation, a micturition cystogram, and an intravenous pyelogram were obtained.

### Material

Of the 1129 patients who were not cured by drugs or operation, 602 were males and 527 were females. At the time of follow-up the youngest patient was 15 and the oldest 36 years of age. Of the 1129 patients, 629 (56%) had primary nocturnal enuresis, 243 (21%) had primary nocturnal and diurnal enuresis, 178 (16%) had secondary nocturnal enuresis, and 79 (7%) had secondary nocturnal and diurnal enuresis (Table I). Of the 1129 patients, 109 (10%) were wetting 2 to 4 nights per week, 123 (11%) 5 to 6 nights per week, and 897 (79%) 7 nights per week, as judged by the initial 8-week record of wet and dry nights, which we felt was more reliable than the mother's history (Table II).

The age of onset of bed-wetting in secondary nocturnal and secondary nocturnal and diurnal enuresis

TABLE I

*Incidence of the various types of enuresis according to sex*

Type of enuresis	Males	Females	Total (and %)
Primary nocturnal	367	262	629 (56)
Primary nocturnal and diurnal	100	143	243 (21)
Secondary nocturnal	98	80	178 (16)
Secondary nocturnal and diurnal	37	42	79 (7)
Total	602	527	1129 (100)

TABLE II

*Number of wet nights per week of patients at their first attendance*

Number of wet nights per week	2-4	5-6	7
Primary nocturnal	53	75	501
Primary nocturnal and diurnal	15	22	206
Secondary nocturnal	21	21	136
Secondary nocturnal and diurnal	20	5	54
Total	109 (10%)	123 (11%)	897 (79%)

varied from 3 to 10 years with the majority starting between 3 and 7 years (Table III).

### Results

**Urinary infection.** 18 patients had an infected urine at the initial examination; after treatment of the infection only one was cured of enuresis.

**Intravenous pyelogram and micturition cystography.** These were performed on 830 patients using the technique described by Fisher and Forsythe (1954). 754 (91%) were normal and 76 (9%) were abnormal (Table IV).

**Treatment.** All patients were treated with at least two drugs and some with three. Treatment in

TABLE IV

*Abnormalities shown by micturition cystography*

Micturition cystogram	Male	Female	Total
Congenital hypertrophy bladder neck	1	—	1
Diverticulum of the bladder	5	—	5
Meatal stenosis	3	—	3
Neurogenic bladder	2	—	2
Posterior urethral valves	6	—	6
Posterior urethral valves with reflux	9	—	9
Reflux alone			
Unilateral	16	26	42
Bilateral	2	1	3
Reflux with infection			
Unilateral	1	2	3
Bilateral	—	2	2
Total	45	31	76

the form of medicine, tablets, or capsules was given a half-hour before bedtime and a record was kept of the wet and dry nights during treatment and during the 8-week follow-up period. Each patient was given treatment for 8 weeks and, if there was a greater than 50% reduction of the wet nights, the treatment was continued for a further 8 weeks. Most drugs recommended for the treatment of enuresis were tried on 50 to 100 or more patients before rejection. They were as follows.

**Atropine-like action.** Tincture of belladonna, homatropine, and phenobarbitone (Peptacol), oxyphenyclimine hydrochloride (Daricon), hyoscyamine, atropine, and phenobarbitone (Donnatal).

**Anti-cholinergic.** Propantheline bromide (Probanthine). Propantheline bromide and phenobarbitone.

**Ephedrine and amphetamine-like.** Ephedrine, methylephedrine (Metheph), methylamphetamine hydrochloride (Metamustac).

**Tranquillizer.** Hydroxyzine hydrochloride (Atarax).

**Diuretic.** Cyclopentiazide (Navidrex).

TABLE III

*Age of onset of bed-wetting for the two types of secondary nocturnal enuresis*

Age (yr) at onset of bed-wetting	3	4	5	6	7	8	9	10	Total
Secondary nocturnal	58	40	36	10	18	5	4	7	178
Secondary nocturnal and diurnal	36	14	10	11	7	1	—	—	79
Total	94	54	36	21	35	6	4	7	257

*Miscellaneous.* Orphenadrine hydrochloride (Disipal).

None of the patients stopped bed-wetting completely while on any of these drugs, except for 25 (34%) of the 106 children treated with propantheline bromide (Probanthine). 8 to 37% of the patients treated with the above drugs had a greater than 50% reduction of the wet nights while on treatment, but they relapsed when treatment was withdrawn. When a controlled trial of (a) propantheline bromide, (b) propantheline bromide and phenobarbitone, and (c) placebo was undertaken on 300 patients, the result was somewhat different, namely 10 (13.9%), 7 (9.0%), and 6 (7.2%) patients were cured, respectively (Wallace and Forsythe, 1969). Statistical analysis showed no significant difference between the three treatment groups, thus emphasizing the unreliability of a pilot trial as compared with a controlled trial. 24 patients cured in the pilot trial and 13 cured in the controlled trial relapsed within 4 months of stopping treatment and have been included in the present series. The remaining 11 patients have been excluded. Additional treatments, e.g. psychotherapy, 'enthusiasm,' raising foot of bed, pelvic floor exercises, lifting by parents etc., when compared with no treatment on groups of 50 to 100 children yielded no significant improvement. A reward system with stars was compared with a plain record card on 100 children and there was little difference between them.

The average annual spontaneous cure of bed-wetting for nocturnal and nocturnal and diurnal enuresis is shown in Table V. The average annual spontaneous cure rate between 5 and 9 years was 14%, between 10 and 14 years 16%, and between 15 and 19 years 16%. 33 (3%) of the patients were still wetting at 20 years of age. It is not possible to give annual spontaneous cure rates after 20 years of age because not all the patients have been followed for the same length of time, though we know that 3 became dry before 22, 4 before 25, and 5 before 30 years of age.

Of the 243 patients with primary nocturnal and diurnal enuresis, 148 (61%) stopped wetting during

the day 3 to 30 months before bed-wetting ceased, 62 (26%) stopped wetting by day and night at approximately the same time, and 33 (13%) continued to wet by day after bed-wetting ceased.

### Discussion

It is surprising that there are so few reports of the incidence of spontaneous cure of nocturnal enuresis. A review of published reports revealed only two such series, Thorne (1944) 161 patients, and Arlien-Soborg (1971) 83 patients. Lovibond (1964) was able to calculate the annual spontaneous cure rate for 1648 patients reported by Bransby, Blomfield, and Douglas (1955), and we were able to do the same for 60 patients reported by Barbour *et al.* (1963) (Table VI). It will be seen from Table VI that the average spontaneous cure rate between 5 and 9 years for the four series was 13%, our figure being 14%. Davie, Butler, and Goldstein (1972), in their comprehensive follow-up, found that 11% were bed-wetting at 5 years and 10% at 7 years, which gives an average annual spontaneous cure rate of 5% for this age period: between 10 and 14 years the average annual spontaneous cure rate for the four series was 19%, our figure being 16%. Between 15 and 19 years the average annual spontaneous cure rate for two of the series was 22% if Barbour's series is excluded, and 31% if it is included, our figure being 16%. It is difficult to compare cure rates for patients over 20 years of age because there is little information, and our own patients have not all been followed for the same length of time. Arlien-Soborg, in her series of 83 patients, found that 13% became dry between 20 and 24 years, 4% between 25 and 27 years, while 17% were still bed-wetting after their 28th birthday. Thorne found during the last war that 2.5% of American draftees were still bed-wetting at 18 years and 1% at 20 years of age. In our series 33 patients (3%) were still bed-wetting at 20 and in the Arlien-Soborg series, 34%.

An organic cause for enuresis is frequently reported, but in our series of 830 patients, plus an additional 530 children not included in the present series that were examined by intravenous pyelo-

TABLE V

*Spontaneous cessation of bed-wetting by age expressed as percentages for nocturnal and for nocturnal and diurnal enuresis*

Age of patient (yr)	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Primary nocturnal enuresis (%)	14	15	15	15	12	17	17	14	17	15	17	15.5	16	15	17.5	16
Primary nocturnal and diurnal enuresis (%)	15	13	15	13	14	15	17	16	17	17	15	17.5	16	15	15.5	16
Average for both (%)	14.5	14	15	14	13	16	17	15	17	16	16	16.5	16	15	16.5	16

TABLE VI

*Annual spontaneous cure rates of nocturnal enuresis (expressed as %) by various authors, giving mean rate for each 5-year period*

Age (yr)	Thorne (1944) 161 patients (%)	Lovibond (1964) 1648 patients (%)	Barbour <i>et al.</i> (1963) 60 patients (%)	Arlie-Soborg (1971) 83 patients (%)	Present series 1129 patients (%)	
5	8	23	3	17	14	
6	13	21	4		14	
7	12	19	2		15	
8	11	19	3		14	
9	3	18	16		13	
10	14	18	16		16	
11	12	17	16		17	
12	17	10	13		15	
13	15	17	15		16	
14	15		50		16	
15	15		45	16		
16	10		33	17		
17	23		75	16		
18	35		—	15		
19	16		100	16		
20	18			16		
Not cured at 20 years	1				34	3

graphy and micturition cystography, the incidence of an organic cause for this complaint was less than 1%. Though Campbell (1970) has stated that 5 to 10% of children have anomalies of the genitourinary tract, we fail to see how most of the anomalies can cause enuresis, e.g. urethral reflux or bladder diverticulum. One of our male patients with multiple bladder diverticula, who is now 26 years old, became dry at night at 19 without surgical interference (Forsythe and Smyth, 1959). In regard to posterior urethral valves, in the 1950s there were differences of opinion about their radiological appearances. 6 of the children included in the series of 35 children with posterior urethral valves, reported by one of us, had mucosal folds and not valves (Forsythe and McFadden, 1959). It might be thought that the symptoms and signs associated with posterior urethral valves, e.g. difficult or hesitant micturition, frequency, and dribbling since birth etc., are so clear cut that they should be recognized without difficulty. But in our experience most parents rarely observe their child voiding after the age of 4, and a urethral obstruction is seldom suspected during micturition cystography until the films are developed. The bladders of patients with moderate urethral obstruction can compensate for a long time, provided no urinary infection develops. Hinman and Kutzmann (1925) reported a case successfully treated at 57 years of age, and Iverson (1914) reported an 85-year-old man who was found to have posterior urethral valves at necropsy. The question then remains to be answered, should we subject all enuretics to

radiological examination in order to find these cases? Since 1963 we have confined radiological investigations to those patients who fail to respond to adequate treatment with the electric alarm (Forsythe and Redmond, 1970) or where the act of micturition was abnormal. 16% of our patients, not included in the present series, treated by the electric alarm were not cured, and of these 6 (10%) had anomalies of the genitourinary tract, none of which was causing the enuresis.

Starfield (1967) and Esperanca and Gerrard (1969) state that bed-wetters frequently have a functional small capacity bladder. In our series of 830 micturition cystograms we thought that 21 patients had small capacity bladders. However, when the cystogram was repeated 6 months to a year later, using a 50 ml syringe instead of a 20 ml syringe, a more even injection rate, and a warmed contrast medium, the bladder capacity was normal in all.

Cystoscopy has seldom provided us with information that could not be obtained by urine analysis and micturition cystography. Though Campbell (1970) states that urethrotrigonitis is the most common finding in enuretic girls, we have seen similar appearances in 11 girls who never had enuresis and where repeated examination of the urine was normal. The few cures reported after urethroscopy and cystoscopy may have been due to the dilatation of the urethra with bougies before passing the urethroscope and/or cystoscope, a method of treatment recommended by Winsbury-White (1941). 13 of the 17 children cured by operation, excluded from the present series, may have been cured by the

preliminary dilatation of the urethra. The 4 remaining children were girls who had ectopic ureters opening into the urethra.

In children with primary nocturnal enuresis, treatment of a coexistent urinary infection has not cured the enuresis. In those with secondary nocturnal enuresis of more than a year's duration and a urinary infection, a few cures of enuresis were obtained after treatment of the infection.

Numerous drugs have been recommended for the treatment of bed-wetting, but the results obtained from well-conducted controlled trials have been most disappointing. The few reported cures may have been spontaneous and not due to the drug or placebo. In addition to the 1129 children included in the present series, a further 779 children with nocturnal enuresis, wetting 6 to 7 nights a week, have been subjected to three controlled trials with the psychoactive drugs imipramine (Tofranil), nortriptyline (Allegron) (Forsythe and Merrett, 1969), amitriptyline and chlordiazepoxide (Limbitrol), and trimipramine (Surmontil) (Forsythe, Merrett, and Redmond, 1972). The few cures obtained did not differ significantly between the drug and placebo. In cross-over trials a 'significant reduction' in the number of wet nights is frequently reported, but this is small comfort to the harassed mother who wants a complete cure and nothing less. There is no doubt that some of the more recent psychoactive drugs, e.g. nortriptyline (Allegron), imipramine (Tofranil), and amitriptyline and chlordiazepoxide (Limbitrol) do produce a significant reduction in the number of wet nights as compared with placebo, but it is not understood how they act and if they act in the same way. Drug therapy would be of value if it cured those patients (10-20%) who fail to respond to adequate treatment with the electric alarm (Forsythe and Redmond, 1970). Unfortunately, most of these patients have to wait for a spontaneous cure.

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Correspondence to Dr. W. I. Forsythe, Department of Paediatrics, The General Infirmary, Great George Street, Leeds 1.