

## POSTERIOR PITUITARY SNUFF TREATMENT OF NOCTURNAL ENURESIS

BY

F. G. W. MARSON, M.D., M.R.C.P.  
*Lecturer in Medicine, University of Leeds*

It is not proposed to review the vast literature dealing with the causation and treatment of nocturnal enuresis. For the purpose of this article it will suffice to state that adolescent and adult sufferers exist in whom no obvious psychiatric or physical disorder can be found, and in whom accepted measures of treatment are of little value. Many such patients also suffer nocturnal frequency, and it is apparent that they have either relative nocturnal polyuria or that their bladders have a subnormal capacity. Such patients might be expected to benefit by a reduction in urine formation during sleep. The use of pituitrin snuff in cases of diabetes insipidus was first reported in 1924 by Choay and Choay; and Vidgoff (1932) and Smith (1934) reported full control of this condition by the use of snuff at eight to ten-hour intervals. It is well known that pituitrin has a similar depressant effect on the urine flow in normal persons (Gutmann, 1928).

Bonacorsi (1925), Blau (1926), and Jacobs (1930) reported the use of pituitrin in the treatment of nocturnal enuresis in children. It is difficult to understand the mode of action of the drug in these cases, as good results were stated to have followed short courses of injections of the drug. More recently, Hansen (1954) has reported satisfactory treatment of nocturnal enuresis by nightly administration of posterior pituitary snuff ("di-sipidin"). He found the results less satisfactory in small children. In none of these reports has the effect of pituitrin been contrasted with placebo therapy, and thus the possibility of a psychotherapeutic effect has not been excluded.

In the present study, four adolescent patients have been treated with pituitrin snuff or placebo snuff over periods of seven to eleven months. They are a special group in that each patient had persistent and frequent nocturnal enuresis, was normal on physical examination, appeared on general assessment to be of normal intelligence, and showed no marked psychiatric disorder. Throughout the period of study the patients kept a strict chart showing each night when enuresis or frequency occurred. The patients were seen every two to four weeks, and at each visit they received a sealed prescription for either pituitrin or placebo snuff, and this was dispensed at the hospital pharmacy. The patients were informed that different types of snuff would be prescribed, but did not know when a change was made or that placebo snuff was being given. The placebo snuff was identical in appearance to the pituitrin snuff. Each patient was instructed to avoid fluids within three hours of sleep, and immediately before retiring to bed a large pinch of snuff was inserted well into each nostril. (The dose was approximately 100 mg.)

### Case 1

A sensitive and intelligent girl aged 19, a printer, was first seen on April 26, 1954. She complained of lifelong bed-wetting, usually occurring one to three times a week. The longest remission prior to present treatment had been for six weeks, and occurred three years previously. A large

quantity of urine was voided when enuresis occurred. She had always been a very deep sleeper and was never awakened by the discomfort of a full bladder or by incontinence. She had received various forms of medical treatment in the past without effect. She had tried avoiding fluids for four hours before sleep, but this measure was ineffective. There was no history of serious illnesses or any family history of enuresis. The prospect of enuresis persisting into adult life naturally caused considerable anxiety to the patient, but she was otherwise free from worries and enjoyed a happy social background. She normally slept from 10.30 p.m. until 6.30 a.m. On examination there were no abnormal physical findings. The urine was free from sugar and contained a trace of albumin. Microscopy of the urine was normal, as was an intravenous pyelogram.

No fluids were taken after 6 p.m. Within the period April 26 to December 5, 1954, pituitrin snuff was administered intermittently for a total of 26 weeks (182 days); during this time nocturnal enuresis did not occur on a single occasion. She received placebo snuff during six weeks (June 14 to July 5 and October 18 to November 8), and during these periods nocturnal enuresis occurred on 21 occasions (50% nights).

### Case 2

A girl aged 15, a factory worker, was first seen on November 23, 1953. She complained of lifelong bed-wetting, usually occurring five or six times a week, a large quantity of urine being voided. She had always been a very deep sleeper and could not be awakened by a loud alarm clock. During a period in which she received amphetamine sulphate in a dosage sufficient to cause insomnia, the enuresis had been largely replaced by nocturnal frequency. Apart from this she had never experienced a remission for longer than two days. She had also suffered from lifelong diurnal frequency, which had been an embarrassment to her at school. There was a previous history of pink disease in the first year, attacks of migraine since the age of 4, and a mastoidectomy at 11. There was no family history of enuresis. She confessed to a certain amount of friction between her mother and herself, no doubt accentuated by the frequent bed-wetting, but was otherwise a happy person with enuresis as her only serious worry. She normally slept from 10.30 p.m. to 7 a.m. Examination revealed a small girl of average intelligence. There were no abnormal physical findings. The urine was free from albumin and sugar, and on microscopy was normal.

No fluids were taken after 7.30 p.m. Within the period November 23, 1953, to November 1, 1954, pituitrin snuff was administered for a total of 37 weeks (259 days); during this time nocturnal enuresis occurred on 10 occasions (3.9% total nights). On four of these occasions the patient had a coryza with profuse nasal discharge and she was unable to retain the snuff properly. She received placebo snuff for a total of nine weeks (January 18 to 25, 1954; May 17 to June 14; and November 1 to 29); during this time, when no coryza occurred, she had nocturnal enuresis on 19 occasions (30.2% nights).

### Case 3

A youth aged 18, a fitter, was first seen on April 5, 1954. He complained of lifelong bed-wetting, which usually occurred from two to seven times a week, a large quantity of urine being voided. His longest remission had been for ten days. He had always been a very deep sleeper. The avoidance of fluids for four hours before sleep had proved ineffective. There was no history of serious illnesses or any family history of enuresis. Apart from the enuresis the patient said that he was free from worries and had a happy home background. He normally slept from 11.15 p.m. to 6 a.m. On examination there were no abnormal physical findings. The urine was free from albumin and sugar.

No fluids were taken after 7 p.m. Within the period April 5 to November 29, 1954, pituitrin snuff was administered

for a total of 30 weeks (210 days); during this time nocturnal enuresis occurred on 10 occasions (4.8% total nights). The patient volunteered that the quantity of urine voided into the bed was much diminished. He received placebo snuff during six weeks (May 10 to 24 and October 4 to November 1), and during this period nocturnal enuresis occurred on 10 occasions (23.8% nights). After both periods when placebo snuff had been given the patient remarked, "This last snuff was not as good as the previous stuff." He based this upon the increased frequency of enuresis and the quantity of urine passed.

#### Case 4

A youth aged 16, a clothing warehouse assistant, was first seen on April 12, 1954. He complained of lifelong enuresis, usually occurring once or twice a week, the longest remission having been for two weeks. He had also suffered from lifelong nocturnal frequency, which occurred once or twice nightly, except when replaced by enuresis. If, however, he did not awaken during the night there would be an even chance of enuresis occurring. There was no past history of serious illness and no family history of nocturnal enuresis. While naturally perturbed by the persistent bed-wetting, he was otherwise free from worries and had a happy social background. He normally slept from 10.30 p.m. to 6.30 a.m. Examination revealed a boy of average intelligence and asthenic build. There were no abnormal physical findings. The urine was free from albumin and sugar. An intravenous pyelogram was normal.

No fluids were taken after 7 p.m. Within the period April 12 to November 29, 1954, pituitrin snuff was taken

TABLE I.—Incidence of Nocturnal Enuresis and Nocturnal Frequency during Administration of Pituitrin Snuff and Placebo Snuff in Case 4

Snuff	Duration in Days	Nocturnal Enuresis		Nocturnal Frequency		No Incident	
		Nights	%	Nights	%	Nights	%
Pituitrin	182	10	5.5	81	44.5	91	50.0
Placebo	49	9	18.4	31	63.2	9	18.4

for a total of 26 weeks (182 days); during this time nocturnal enuresis occurred on 10 occasions (5.5% total nights), nocturnal frequency on 81 nights (44.5% total), and on the remaining nights (50%) he slept without incident (see Table I). He received placebo snuff for seven weeks (July 19 to September 6), and during this period nocturnal enuresis occurred on nine occasions (18.4% total nights), nocturnal frequency on 31 nights (63.2% total), and he slept without incident on nine nights (18.4% total).

#### Analysis of Results

The difference in frequencies of nocturnal enuresis during administration of pituitrin and placebo snuff were worked out by "2 x 2" tables, making use of  $\chi^2$  method (Fisher, 1946). Table II shows the results. In Cases 1, 2, and 3,  $P < 0.001$ , which indicates that the possibility of the results being a chance finding is less than one in a thousand. In Case 4  $P < 0.01$ , indicating that the possibility of a chance finding is less than one in a hundred. It is clear that in

TABLE II.—Analysis of Incidence of Nocturnal Enuresis in Four Adolescent Patients during Total Period in which they Received either Pituitrin or Placebo Snuff

Case No.	Snuff	Wet Nights	Dry Nights	$\chi^2$	P
1	Pituitrin	0	182	100.4	<0.001
	Placebo	21	21		
2	Pituitrin	10	249	42.8	<0.001
	Placebo	19	44		
3	Pituitrin	10	200	17.38	<0.001
	Placebo	10	32		
4	Pituitrin	10	172	8.48	<0.01
	Placebo	9	40		

all four cases there is a marked reduction in the incidence of enuresis during pituitrin treatment, the reduction being very highly significant in the first three patients.

#### Discussion

The list of therapeutic measures—medical, surgical, and psychiatric—bears witness to the relative inefficacy of any one of them in the treatment of nocturnal enuresis. Although first suggested by Bonacorsi (1925), the use of pituitrin in the relief of this condition has received scant attention in the literature. This is surprising, as the well-known effect of pituitrin in reducing the urine output might reasonably be expected to benefit certain patients. Hansen (1954), has reported satisfactory results with pituitrin snuff in older children and adults, and cites one case in which the incidence of nocturnal enuresis was reduced from nightly to once or twice a month.

This present study has been limited to four adolescent patients, comprising a selected group in that they were all of average intelligence, had a satisfactory social background, and were free from obvious physical or psychiatric defect. The possibility of a psychotherapeutic effect has been excluded by comparing the results obtained with pituitrin snuff with those during placebo administration. A reduced incidence of enuresis occurred in each patient during the periods in which pituitrin snuff was taken each night. The most favourable response (Case 1) consisted in complete relief from nocturnal enuresis during 23 weeks in which pituitrin snuff was taken, enuresis occurring frequently during the two periods in which placebo snuff was substituted. One patient suffered nocturnal frequency as well as enuresis, and a reduced incidence of both symptoms was observed during pituitrin therapy (see Table I). No untoward effects were experienced during this study, and the only difficulty in administration was observed in the one patient who was unable to retain snuff completely in the presence of a coryza.

Pituitrin snuff is variously reported as acting for five to ten hours, and the shorter the period of sleep the more effective cover it should give. It may well prove of little value in children requiring upwards of 12 hours' sleep, but in adolescents and adults sleeping for eight to nine hours its effect is likely to persist for most of this time and should thereby effect an overall reduction in urine production during the period of sleep.

The results leave little doubt about the effectiveness of this form of treatment in the cases studied. They support Hansen's findings and suggest that pituitrin snuff therapy deserves a full trial in any adolescent or adult patient failing to respond to other forms of treatment.

#### Summary

Four adolescent patients with nocturnal enuresis have been treated with pituitrin snuff for six to nine months, and the results have been compared with those observed during the administration of a placebo snuff. Although obtained from a small series of selected cases, the results suggest that pituitrin snuff will prove of great value in the treatment of certain adolescent and adult cases of nocturnal enuresis.

I wish to thank Dr. W. MacAdam for referring Case 1; Dr. J. G. Dare for advice on the statistical analysis; and Professor R. E. Tunbridge for his helpful criticism in the preparation of this paper. I am indebted to Messrs. Paines and Byrnie Ltd. for the supplies of "di-sipidin" and the placebo snuff.

#### REFERENCES

- Blau, A. I. (1926). *Med. J. Rec.*, 124, 492.  
 Bonacorsi, L. (1925). *Pediatrics (Napoli)*, 33, 936.  
 Choay, A., and Choay, L. (1924). *Rev. neurol. (Paris)*, 31, 267.  
 Fisher, R. A. (1946). *Statistical Methods for Research Workers*. 10th ed. Edinburgh and London.  
 Gutmann, K. (1928). *Arch. Verdaukr.*, 42, 551.  
 Hansen, R. E. A. S. (1954). *British Medical Journal*, 1, 1038.  
 Jacobs, F. B. (1930). *Penn. med. J.*, 33, 388.  
 Smith, F. M. (1934). *J. Amer. med. Ass.*, 102, 660.  
 Vidgoff, B. (1932). *Endocrinology*, 16, 289.