ENURESIS AS A DISORDER OF DEVELOPMENT

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The concept of enuresis as a primary delay in development of bladder control is not new (Denny-Brown and Robertson, 1933), but much effort has been expended in order to find other physical or emotional causes for this symptom. Bakwin (1961) has pointed out the unsatisfactory nature of the evidence for such causes and has re-emphasized the fact that enuresis tends to disappear with increasing age and has a striking familial incidence. We have not found in the literature an investigation attempting to make a comprehensive assessment of a series of enuretic children which also includes a follow-up study. The study reported here provides evidence regarding the effects of maturation in a series of comprehensively investigated children.

Material and Methods

In a 12-months period during 1951-2 children with enuresis attending the Bristol Royal Hospital for Sick Children were, by arrangement with the consultants concerned, referred to one of us (M. M. B.) for investigation. Preliminary selection of the cases had been made by the family doctor or local authority medical officer; but once referred to the medical, psychological, or urological clinics they were put consecutively into the study. Cases were accepted only if bed-wetting was the major complaint and if the patients had attained the age of 5 years.

A total of 111 cases entered the study, and the initial assessment was designed to be comprehensive. A full medical, psychological, and social history was obtained by M. M. B., who also performed the physical examination and cystometry. Psychological assessment included not only the history from the parents but also observations on the child's behaviour and personality in the ward, and a school report was obtained. Intelligence-testing and electroencephalography were done by the specialist departments. Urological examination included cystoscopy, radiological examination included intravenous pyelography, but cystourethrography was done only if indicated.

Treatment was individualized according to the results of the assessment. All the patients were given an explanation of the condition, and the majority received medication in the form of ephedrine or belladonna. If a severe degree of obstruction of the bladder neck with troublesome frequency and urgency was present a transurethral resection was performed, and a few cases received intensive psychiatric treatment. Conditioning devices were not in use at this time. The duration of treatment under hospital out-patient supervision was in most cases quite short and many lost touch after a few months.

Five years after the initial assessment it was decided (R. F. B. and T. E. O.) to trace the children and ascertain whether they still had symptoms. The follow-up assessments were made by E. M. B. and T. E. O. It was neither possible nor justifiable to repeat all the investigations, but information obtained included the degree of bladder control

achieved, the age at which dryness had occurred, an assessment of puberty status, and the social and psychological climate at home, school, or employment.

Of the 111 children in the original study, eight were excluded because of severe or progressive neurological or urological disease (ectopic ureter, chronic pyelonephritis, neurogenic bladder) and 10 could not be traced or were unavailable for follow-up. The remaining 93 children were seen and form the material for this paper.

There were 62 boys and 31 girls, whose ages at the initial assessment ranged from 5 to 14 years. Bed-wetting had been lifelong in 74 cases, and in most of the 19 cases in which a dry spell had been reported the enuresis had started at under the age of 3 years. The social class and I.Q. distributions were:

Social class: I (8%); II (6%); III (34%); IV (28%); V (24%)
I.Q.: 65 (1%); 65- (2%); 75- (26%); 90- (47%); 110- (23%);
125+ (1%).

These figures probably indicate the degree of selection of cases rather than the distribution of enuresis in the population. However, it is clear that there is no bias towards very dull or socio-economically impoverished children.

The majority of children came from normal homes and were members of stable family groups; there was no excess of neurotic traits, or personality or behaviour difficulties, and their school performance was not very much below their expected potential. Most were in good physical health, but half of them had symptoms of frequency, urgency, or occasional day wetting in addition to the nocturnal enuresis. Their parents had reacted in various ways to the symptoms, usually either punitively or anxiously, and most of the patients had been subjected to a variety of domestic punishments and treatments before referral. No consistent patterns were discernible: detailed reference is made to some of these factors later.

Results

At follow-up it was found that 37 (60%) of the boys and 23 (74%) of the girls had become "dry" as defined by cessation of bed-wetting for at least two months prior to the follow-up interview. The age at which the symptom had disappeared in the dry group is shown in Fig. 1.

Eighteen (49%) of the boys and 12 (52%) of the girls who became dry during the study did so by the age of 12 years. By 15 years 28 (75%) of the boys were dry, and 17 (74%) of the girls were dry by the age of 14. The parents of the dry children attributed cure to a variety of reasons, but in only one-third of the cases was medical intervention thought to be the cause.

Further evidence of the overriding importance of age and the relative ineffectiveness of standard therapy is given in Fig. 2, in which the age and sex distribution of the series is shown together with the outcome at follow-up.

It is apparent that those entering the study at the young ages are those who are likely to be wet five years afterwards, while those presenting later are more likely to be dry, as would be expected if therapy has little influence on the disorder; it does not bear out the suggestion that bed-wetting of long duration has a poor prognosis.

FIG. 1.—Histogram showing age at which 60 children who became dry during the period of study attained bladder control. Boys are indicated above the baseline, girls below.

FIG. 2.—Histogram showing that cases entering the study in the age-group 5-9 years are more likely to be "wet" five years later than those entering at 10+ years.

The effect of age makes it impossible to compare directly the "wet" group with the "dry" group. However, it is reasonable to analyse further the children who had passed their fifteenth birthday at the time of follow-up. Fifty adolescents (over 15 years old) are available, 16 of whom are "persistent" bed-wetters and 34 "dry" (Table I). The "persistent" group is that most likely to reveal important aetiological factors in enuresis which may dominate the effect of development, and this group has been compared with the whole series and the "dry (over 15 years)" group in order to isolate the factors.

TABLE I

	Total	Over 15 Years		
		No.	Persistent	Dry
Boys	62	34	12	22
Girls	31	16	4	12

Family History.—Precise genetic data are not available, but it was ascertained whether enuresis had occurred in parents, sibs, or near relatives (positive) or if enuresis was unknown in either family (negative) (Table II).

The familial nature of enuresis is well demonstrated, but is not apparently more obvious in the persistent group.

TABLE II

Family History	Total	Over 15 Years	
		Persistent	Dry
Positive	60	11	26
Negative	33	5	8

Psychological Factors

For purposes of quantitation we have attempted to summarize psychological factors under three headings—intelligence, adjustment, and home life.

Intelligence.—There is a tendency for the persistent enuretics to fall in the duller group (Table III).

Adjustment.—We classified the material into three categories; normal, slightly maladjusted, and disturbed (Table IV). Assignment to a category was made by decision at meetings of all the investigators after considering the relevant data. The decision was made without knowledge of the outcome of the follow-up visit. It would be misleading to compare our figures with others who have

TABLE III

I.Q. Range	Total (93)	Over 15 Years	
		Persistent (16)	Dry (34)
Less than 65	1	—	1
65-74	2	1	1
75-89	24	6	9
90-109	44	7	14
110-124	21	1	9
125+	1	1	—

TABLE IV

Adjustment	Total (93)	Over 15 Years	
		Persistent (16)	Dry (34)
Normal	54	14	19
Slightly maladjusted	32	2	10
Disturbed	7	—	5

tried to quantitate the part played by emotional disorder in enuresis, but we have attempted to be consistent within our series. There is no evidence that those deemed maladjusted at the initial assessment were more likely to persist. It is also of interest that at follow-up the dry cases did not appear to have developed new symptoms of emotional disorder, and both they and their parents felt that disappearance of enuresis had invariably resulted in improvement in psychological well-being.

Home Life.—In a series of this composition a large number of deprived children would not be expected. The assessment into normal or deprived was largely made on the structure of the family and the relationship within the family group (Table V).

TABLE V

Home Life	Total (93)	Over 15 Years	
		Persistent (16)	Dry (34)
Normal	81	16	31
Deprived	12	—	3

Summarizing the psychological factors, it is not clear that they have played an important part in the problem of enuresis as a whole. It is certain that they are not of special significance in the prolongation of enuresis beyond puberty.

Electroencephalography

An unexplained feature of enuresis is its association with abnormal electroencephalograms. Most of our cases

were included in the report by Turton and Spear (1953), and reference should be made to this paper for their interpretation of the encephalograms. We have followed their classification, and have placed the children into normal, immature, and epileptic groups (Table VI). Whatever the explanation for the abnormal electroencephalographic findings, they are not a necessary feature of the persistent enuretic.

TABLE VI

Electroencephalogram	Total (93)	Over 15 Years	
		Persistent (16)	Dry (34)
Normal	15	3	3
Immature	66	9	27
Epileptic	12	4	4

Physical Factors

Cystoscopy was performed by the consultant urologist. From the cystoscopic evidence it was possible to classify cases as having normal bladders, obstruction of the bladder neck of varying degree, or other (usually funnel-neck) deformity (Table VII).

TABLE VII

Cystoscopy	Total (91)	Over 15 Years	
		Persistent (15)	Dry (33)
Normal	35	5	14
Bladder-neck obstruction	52	9	18
Other abnormality	4	1	1

Children with obstruction of the bladder neck tended to show a rising or high-tension cystometrogram. Ten cases showed a small bladder capacity and in eight this was associated with hypertrophy of the bladder neck and a high-tension cystometrogram. Five children with obstruction of the bladder neck were treated with transurethral resection because of extreme daytime frequency and urgency; all three of these who have reached puberty are still bed-wetters. The high incidence of abnormalities of the bladder neck is difficult to explain; this anatomical abnormality might be a causative factor or be a sequel of the disordered bladder function. In our series, of the 52 children with bladder-neck obstruction 36 (70%) had a positive family history of enuresis, whereas 25 (71%) of those with normal bladder necks had a positive family history. Whatever the explanation it is apparent that abnormalities of the bladder neck are not a decisive factor in the persistence of enuresis, and that many children with hypertrophy of the bladder neck achieve spontaneous cure of enuresis without operative intervention. However, it is rare for an adult enuretic to have a normal bladder (Miller, 1962).

Discussion

Bed-wetting is an inconvenient symptom from which relief is sought by both the affected child and his harassed parents. In a small number of cases the bed-wetting is only one of several symptoms which indicate major organic or emotional illness. A detailed history, adequate physical examination, and urinalysis will usually reveal the presence of the underlying disease, and the necessary treatment can be obtained. In the majority of enuretic children no signs of organic or psychiatric disease are discernible apart from those which spring directly from the bed-wetting habit. The children with whom we are concerned are drawn from this group but represent only those who have failed to become dry by the age of 5 or later and who have resisted the traditional remedies. This group is not necessarily

representative of the total population of enuretic children, but does include the children who present the greatest problem in practice, for which optimal methods of investigation and treatment are by no means clear.

Bakwin (1961) has suggested that the fundamental disorder in the enuretic child is his difficulty in controlling the emptying of the bladder. He believes that this difficulty is a developmental defect largely determined by hereditary factors. This view fits in well with the clinical evidence and is not incompatible with Muellner's (1960) radiological studies which show that the bladder of the enuretic child does not have the normal rapid increase in capacity during early childhood.

Our data support a "developmental" concept of enuresis in that we have clearly shown that the disappearance of the symptom is dependent more upon age than therapeutic intervention and that the abnormalities found by "comprehensive" investigation serve only to delay the gaining of bladder control rather than prevent its occurrence. Negative evidence is adduced from the fact that we have failed to isolate factors of a physical or psychological nature which can be consistently associated with persistent enuresis. This does not preclude the idea that such factors may be present but were not investigated.

However, if the primary "fault" in enuresis is a "learning" defect, perhaps analogous to developmental delays in speech and writing, it might be due to structural or functional immaturity of the neuromuscular pathways subserving bladder control, to errors of learning at the toilet-training era, to inhibition of learning by emotional factors, or to the presence of minor anatomical abnormalities creating increased difficulties in learning. In any individual a combination of the factors may be present.

If the witch hunt for a constant, single aetiological factor, either organic or emotional, is called off, we are left with the opinion that the enuretic child is endowed with "a weak bladder which he will grow out of." In the absence of exact knowledge regarding the organization and development of the complex sensori-motor mechanisms concerned in the acquisition of bladder control it is difficult to be more precise. This rather simple explanation does, however, remove feelings of guilt from the mother who blames herself for "mismanaging" the child and from the child who has almost always been made to feel that he is "lazy," thoughtless, and irresponsible. This concept may also save the already distressed children from the striving of the doctors to put them right by surgical, pharmacological, or psychotherapeutic means. It is, however, a negative explanation in that both mother and child must endure the symptom with patience and hope until such time as "maturation" occurs. The doctor's role need not necessarily be entirely passive, and intervention designed to aid the learning process (conditioning devices, bladder-training) or to remove anxiety and unhelpful parental attitudes may be successful; however, we have no evidence in this study on these points.

The failure to observe within the age-group studied a consistent abnormality or pattern of factors responsible for the persistence of bed-wetting is interesting. From the prognostic viewpoint it would be helpful to be able to identify children likely to remain bed-wetters in adolescence and also to be able to initiate successful therapy at an early stage. However, no outstanding characteristic marked the persistent group, and if such a factor exists we are unaware of it. It is of some practical importance that long duration of bed-wetting, abnormalities of the bladder neck, maladjustment, or deprivation did not act as barriers to spontaneous cure, and there is no reason to give children

with these problems a poor prognosis provided that the disorder is treated in a reasonable way.

Summary

Of 111 children referred to hospital with enuresis who were comprehensively evaluated, 93 were followed up after a period of five years. It was possible, therefore, to determine the number who remained wet five years after initial investigation and treatment and to ascertain the time of cessation of bed-wetting in those who had become dry.

At initial evaluation no single causal factor accounted for enuresis. A positive family history of the condition was frequent and abnormalities in the electroencephalogram were present in 84%. The majority of the children came from stable homes and most of them did not show marked emotional disturbances.

At follow-up 93 children were traced and interviewed: 37 (60%) of the 62 boys and 23 (74%) of the 31 girls had become "dry." Age was more strongly associated with cure than any other factor. A greater percentage of those entering the survey at 10+ years had become "dry" more frequently than of those investigated earlier. Half the series

were dry by the age of 12 years and three-quarters by 14-15 years.

Children whose bed-wetting persisted after puberty tended to be duller than those becoming dry earlier, but no correlation was shown between persistence of enuresis and deprivation, maladjustment, or abnormalities of the bladder neck.

The study has failed to reveal a constant, single cause of bed-wetting, nor has it indicated any particular factor among those commonly considered which is associated with the persistence of enuresis. At present, therefore, it is reasonable to regard enuresis as a delayed development or loss of bladder control which may be affected by many factors, physical and psychological.

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"COLOMYCIN" TREATMENT OF KLEBSIELLA AEROGENES INFECTION OF URINARY TRACT IN PARAPLEGIA

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Recently introduced into this country, "colomycin" (colistin methane sulphonate) is an antibiotic isolated by Koyama *et al.* (1950) in Japan as a fermentation product of *Bacillus colistinus*. In chemical structure and antimicrobial activity it closely resembles the polymyxins, but no serious toxic effects have been reported (Schwartz *et al.*, 1959-60; Wright and Welch, 1959-60). Colomycin is effective in many Gram-negative infections, mainly those due to the *Pseudomonas* and *Klebsiella* groups (Petersdorf and Hook, 1960; Yow *et al.*, 1961; Carroll and Malette, 1961).

Traumatic paraplegia results in an initial period of complete retention of urine, when some form of catheterization is necessary. In the National Spinal Injuries Centre intermittent catheterization is employed as the method of choice in the immediate and early stages following the onset of paraplegia, and is continued until automatic micturition begins and the residual urine is less than 100 ml. Many patients remain free from infection for many weeks during this period of intermittent catheterization, and only a certain number develop an infection of the urinary tract. In the absence of complicating factors, such as stones in the urinary tract, hydronephrosis, or bladder diverticula, treatment with the appropriate antibiotic is generally effective in eliminating the infection and rendering the urine sterile again. An exception is infection due to *Klebsiella aerogenes*, which is often resistant to all the routine antibiotics and is found relatively frequently in this centre. The trial reported here was carried out to determine the effectiveness of colomycin in the treatment of *K. aerogenes* infection of the urinary tract in paraplegia.

Material and Methods

Eighteen male paraplegic patients were selected, all of whom had had persistent *K. aerogenes* infection of the

urinary tract for varying periods from 2 to 60 weeks, the organism having been isolated in pure culture on at least three separate occasions immediately preceding the trial. All patients had persistent pyuria and bacilluria, but were afebrile and free from toxic symptoms. Other antibacterial drugs, such as penicillin, nitrofurantoin, tetracycline, sulphadimidine, and streptomycin, had previously been unsuccessfully tried in all cases. Residual urine in each patient was less than 100 ml. All patients had normal renal function as judged by a normal blood urea at the beginning of treatment and a urinary protein level of less than 10 mg./100 ml.

During the trial no patient was catheterized. Midstream specimens of urine were carefully taken from each patient daily during the course of treatment and at least twice during the week following the end of treatment. All specimens were cultured on blood agar and MacConkey agar, examined microscopically, and tested for protein. The viable bacteria in the urine were counted on the day before treatment began and daily throughout the course of treatment, using the method of Miles *et al.* (1938). Each specimen of urine was examined within one hour of being taken from the patient.

A blood urea estimation was carried out on each patient during the week before onset of treatment and again within a week after conclusion of treatment. Capsular typing of the organism was carried out in each case, and also on any *K. aerogenes* isolated during treatment and the period of follow-up. The minimum inhibitory concentration of colomycin for growth of *K. aerogenes* freshly isolated from each patient was determined before treatment, using doubling dilutions of colomycin in broth. Colomycin blood levels were measured in five patients and urinary levels in eight. The levels were determined by serial dilu-