Summary

A case is described of severe post-partum haemorrhage due to cervical laceration in a grand multipara.

The laceration extended into the lower uterine segment extraperitoneally without evidence of this when the hand explored the uterus.

The lesson is emphasized that a case of post-partum haemorrhage with a contracted uterus must be examined most carefully under general anaesthesia for high vaginal and cervical tears. Tearing of the cervix or vagina should be suspected when haemorrhage occurs round the head as it is delivered.

After stitching a cervical laceration and packing the uterus the patient's condition should improve when blood is transfused. If it does not, broad-ligament haematoma should be suspected and hysterectomy carried out without waiting for resuscitation of the patient—resuscitation which will not occur until haemorrhage has been arrested.

Intra-arterial transfusion of blood can induce a quick response during operation when the bleeding-points have been secured.

This patient required transfusion of 34 pints (19.3 litres) of blood and two operative procedures before recovery was assured.

REFERENCES

- Artz, C. P., and Howard, J. M. (1954). *J. Amer. med. Ass.*, **156**, 488.
Bunker, J. P., Stetson, J. B., Co, R. C., Grillo, H. C., and Murphy, A. J. (1955). *J. Amer. med. Ass.*, **157**, 1361.
Crosby, W. H., and Howard, J. M. (1954). *Blood*, **9**, 439.
Krevans, J. R., and Jackson, D. P. (1955). *J. Amer. med. Ass.*, **159**, 171.

VALUE OF PROPANTHELINE BROMIDE IN TREATMENT OF ENURESIS

BY

DUNCAN LEYS, D.M., F.R.C.P.

Senior Physician, Paediatric Unit, Farnborough Hospital

There is no simple statement which adequately covers the phenomena of enuresis, whether one is speaking of causation, of mechanisms, or even purely of description. Most people now regard enuresis as a sign of immaturity or as evidence of regression to an immature form of behaviour under the stress of insecurity. The mechanism is much more complex than merely that of lack of continence of the bladder. Intermittent diuresis is apparent in most cases and probably present in all, and this is itself reminiscent of the lack of concentrating power of the infant kidney. The social disability of the symptom in the later years of childhood or in adult life is severe. Winnicott (1953) emphasized the need for "symptom tolerance" in paediatrics, by which he meant a refusal to become enthusiastic in the treatment of symptoms in disregard of the total situation of the sick child. He took as his text the life history of a child in whom enuresis appeared as one symptom of a necessary emotional regression, and showed how inadequately treated such a child would be if, presenting to the doctor through his parents' anxiety on account of the bed-wetting, treatment should be directed solely to the cure of this symptom.

Such limited understanding of enuresis in the life of a child accounts for the fact that not one of the many remedies employed has more than limited success. But

with understanding by doctors, parents, and teachers of the significance of the symptom, and a willingness to make a serious and continuing effort to restore the child's confidence, the symptom itself disappears. Short cuts in the treatment of enuresis are therefore only justifiable if a serious attempt has been made to secure this confidence. Any remedy which is harmless has a place in treatment if its employment is understood to be no more than an adjuvant, a lifting of the secondary burden of discomfort and feeling of social inadequacy, and possibly an encouragement to an understanding mother or guardian. Conditioning apparatus with which rather remarkable success can be obtained (at least in older children) falls into this category, and so do several drugs which it has been customary to use.

The mode of action of such drugs is not clear. Amphetamine, for example, which has some action on the peripheral autonomic nervous system, has a much more profound central action, and its effects in enuretic children are comparable to those which follow its use in psychiatry. Drugs with an atropine-like action have been used in the treatment of enuresis for a century; their mode of action also is central, not a simple peripheral one. Toxicity—that is, undesirable effects not contributing to the anti-enuretic action—limits the use of the naturally occurring drugs of this group, but there are now synthetic analogues which are relatively free from some of these unpleasant effects and which could therefore be tried as adjuvants in the treatment of enuresis, with some prospect of success.

Present Investigation

Propantheline bromide ("pro-banthine") is such a drug. It has been used fairly widely in conditions where it was believed that overaction of the parasympathetic was playing a part in symptom production. In order to see whether any anti-enuretic effect could be obtained, a controlled trial of the drug, used in a dosage which was known to be free of "toxic" symptoms, was undertaken. Eighty-two children took part in the trial, and these were allocated as they presented themselves to one of two groups alternately. Group A, the treatment group, were given propantheline, 15 mg. daily for the first four days, 30 mg. for the next four days, and 45 mg. for six days; group B, the control group, were given as placebo the excipient, without the propantheline, made and packed in exactly the same form by the manufacturer. The identity of the drug and the placebo was not disclosed to anyone taking part in the trial, either patients or staff, until all the results were collected. Eight children in group A and nine in group B failed to complete the trial, leaving 33 in group A and 32 in group B. In both groups, parents and guardians were asked to record wet beds and dry beds for a total period of eight weeks—for two weeks before the tablets were given, for two weeks during the taking of the drug, and for four weeks after it was discontinued. No child under 5 or over 15 was included. The age constitution of the two groups is shown in Table I.

TABLE I.—Age Incidence

Age in Years:	5-7	8-10	11-15	Total
Group A	8	14	11	33
" B	10	14	8	32
Total	18	28	19	65

No child was included who was recorded to have had less than two wet nights during the 14 days of preliminary observation. Of the 65 children completing the test, 29 were "deprived"—that is, separated from their families and living in children's homes; there were 15 of such children in group A and 14 in group B.

Results

The results of this test were assessed by taking the total number of wet beds in the two groups in the two weeks before treatment (period 1), in the two weeks during which the tablets were given (period 2), and in the four weeks after treatment was stopped (period 3). These figures are shown in Table II.

TABLE II.—Results of Test

	Group A (Propantheline)			Group B (Placebo)		
	Dry Beds	Wet Beds	Ratio D/W	Dry Beds	Wet Beds	Ratio D/W
Period 1 ..	118	344	0.343	132	316	0.418
.. 2 ..	152	310	0.490	105	342	0.308
.. 3 ..	269	655	0.410	213	683	0.311

I am indebted to Dr. Louis Griffiths for the following statement on the statistical significance of these figures: "During period 1 there is no significant difference between the treatment and placebo group ($\chi^2=1.8$, $P>0.1$). In period 2 the diminution in the number of wet beds is highly significant ($\chi^2=17.6$, $P<0.01$). The increased number of wet beds due to the placebo is also probably significant ($\chi^2=4.07$, $P>0.02$). In period 3, the post-treatment period, neither group of figures shows significant differences."

It would therefore seem safe to conclude that propantheline bromide, used in this way, has a small (5%) but definite effect in diminishing the number of wet beds in nocturnal enuresis, an effect which disappears (as statistically significant) in the post-treatment period. If individually severe cases only are selected for study—that is, those children showing in period 1 a D/W ratio of less than 0.25—we get

TABLE III.—Results in Severe Cases Only

	Group A (Propantheline) (17)			Group B (Placebo) (16)		
	Dry Beds	Wet Beds	Ratio D/W	Dry Beds	Wet Beds	Ratio D/W
Period 1 ..	12	212	0.057	16	208	0.078
.. 2 ..	31	193	0.139	19	205	0.092
.. 3 ..	36	418	0.086	26	422	0.062

the results shown in Table III. Dr. Griffiths comments: "In period 1 there is no significant difference between the two groups. In period 2 the difference due to treatment is highly significant ($\chi^2=9.1$, P almost reaching the 0.001 level). The differences in period 3 are not significant."

The effect of the propantheline bromide in this group is more emphatic, but it shows no persistence into the post-treatment period. No child was cured; but cures were, of course, hardly to be expected, since the drug was used for quite a short time and the dosage used was empirical. In using amphetamine in the treatment of enuresis it is customary to give the maximum dosage—for example, up to 20 mg. a day for four to eight weeks—before concluding that the drug is of no value; thus there should be relative optimism concerning results to be expected when propantheline bromide is used in rather larger doses and for longer periods.

There is no sex bias in the incidence of enuresis, but in the present series there was a rather large preponderance of boys, owing to the fact that all the "deprived" children came from boys' homes. There is, however, no significant difference in the results of treatment when the sexes are compared.

Pharmacology

Propantheline is 2'-diisopropylaminoethyl xanthen-9-carboxylate methobromide. It is described as an "autonomic blocking agent" (acetylcholine inhibitor) or, in other words, as an anticholinergic drug. Its potency, in various forms of trial, is two to three times greater than that of atropine. Its essential effects are those of atropine—decreasing salivary and gastric excretion, and (in sufficiently large dosage)

causing acceleration of the pulse, constipation, blurring of vision, and retention of urine. In therapeutic dosage such effects are quite exceptional, and none of the children in this trial were reported to have been upset or to have shown any toxic symptoms at all. In extreme overdosage in animals, a curare-like action is apparent; a lethal dose in rats (LD50) is about 1,000 mg. per kg. One-tenth of the minimal lethal dose was given to rats daily for some months without any observed effects except in slowing the rate of growth.

Summary

A controlled trial of propantheline in the treatment of 65 enuretic children is described.

The drug was found to have a limited but definite action in reducing the number of wet beds in enuresis, and as an adjuvant to the full consideration of the individual child suffering from this complex condition to have a definite place in treatment.

My thanks are due to Messrs. Searle and Co. for supplies of "pro-banthine" and for their full co-operation during the trial; to Miss Elizabeth Harvie, children's officer for the County of Kent, for her help in obtaining the co-operation of superintendents of children's homes; and especially to Miss Kathleen Minchin, secretary to the Children's Department, Farnborough Hospital, who undertook most of the tedious work of collecting and abstracting the reports.

REFERENCE

Winnicott, D. (1953) *Proc. roy. Soc. Med.*, **46**, 675.

A CONTROLLED TRIAL OF PROPANTHELINE IN BED-WETTING*

BY

R. M. MAYON-WHITE, M.D., Ph.D., M.R.C.P.
D.C.H.,

Consulting Paediatrician, Children's Department,
Ipswich and East Suffolk Hospital

It is the purpose of this paper to report the result of a small controlled trial of propantheline ("pro-banthine") in the treatment of simple nocturnal enuresis.

The literature on bed-wetting reveals many different therapeutic regimes based on many different theories of aetiology, and many empirical routines based on no particular theory but justified by the results obtained. It is a disappointing feature of most of the papers that little attempt is made to control the various factors that may influence the results of treatment. The critical reader is left with an uneasy feeling that the doctor's confidence in his treatment has played an important part, and that perhaps indirect psychotherapy by suggestion is responsible for the successful cases. This dearth of controlled experiment is the more disappointing because the results of treatment are so easily seen: there can be little observer error about a wet bed or a dry one.

For many years atropine preparations have been thought to be of value in relieving frequency and urgency of micturition and have been in vogue for a long time in the treatment of enuretic children. Recently methantheline ("banthine") and propantheline have been widely used in urinogenital surgery. The pharmacological activity of these substances (an anticholinergic effect) upon the normal and neurogenic bladder has been demonstrated (Keizur and Hodges, 1953). By producing

*A summary of this paper was communicated to the East Anglian Paediatric Club on October 1, 1955.