# THE ABSENT TESTICLE

## A REPORT ON A SURVEY CARRIED OUT AMONG SCHOOLBOYS IN NOTTINGHAM

BY

**BARBARA WARD, M.B., D.A., D.C.H.**

AND

**WILLIAM MACMILLAN HUNTER, M.B., Ch.B.**

*School Medical Officers to the City of Nottingham Education Committee*

It is not uncommon to find at routine medical examinations of schoolboys that one or both testicles appear to be absent from the scrotum. This poses the problem of whether the testicle is undescended, maldescended, or retracted—a problem which becomes more serious as the child grows older.

Climatic conditions, the temperament of the child, an active cremasteric reflex, and other factors may prevent the doctor from palpating a retracted testicle. A maldescended testicle may be felt superficially above the inguinal ligament, while a truly undescended testicle cannot be palpated inside or outside the scrotum. In the past, various methods of treatment have been undertaken. Physicians have often given a series of hormone injections in order to hasten sexual development and produce a descent of the testicle; and endeavours have also been made to bring about its descent surgically, the success of this procedure depending on the blood-supply and the length of the spermatic cord. In the opinion of others it is held that treatment is unnecessary until puberty is imminent, the view being taken that the undescended testicle often descends unaided.

It is therefore a matter of some importance to determine, if possible, the natural history of the undescended testicle, and to find out when, if at all, treatment is necessary.

Several surveys have been made in the past in an endeavour to throw light on this problem. Scorer (1955, 1956) examined some 1,500 babies after birth and again after the lapse of a year. He found 3.4% to have undescended testicles. A number of reports (Coley, 1919; McCutcheon, 1938; Smith, 1941) have been made concerning boys above and below 15 years of age. Of these, 3.3 to 9.4% under 15 years and 0.6 to 0.8% over 15 years had undescended testicles. In 1956–7 a survey (Society of Medical Officers of Health, 1958) was made among schoolboys in East Anglia between the ages of 5 and 17 years which gave the following results: 4% of the boys of 5, 8, and 11 years showed unilateral undescended testicles and 2% showed bilateral undescended testicles; the average proportion among school leavers aged 14–17 years was found to be 0.6% undescended on one side and 0.1% on both sides. A marked variation was noted among the findings of the several doctors taking part in the survey. It was difficult to determine by one examination alone whether an apparently undescended testicle was actually undescended or merely retractile.

### Present Survey

This survey was conducted during 1957–8 by five medical officers in the schools of the Nottingham Education Committee. At the routine examination of 19,024 boys aged 5, 8, 11, and 14–17 years unilateral and bilateral undescended testicles were noted. The figures are shown in the accompanying Table. It is seen that the total incidence of unilateral and bilateral undescended testicles in 1957 rises from 2.29% at 5 years to 6.23% and 5.42% respectively at 8 and 11 years, falling to 0.41% at 14–17 years. In 1958 there were 1.15% of undescended testicles at 5 years, rising to 2.40% and 4.05% at 8 and 11 years, and falling to 0.23% at 14–17 years. Boys who had received any form of treatment were not included in the figures.

*Results of Routine Examination of 19,024 Boys Aged 5, 8, 11, and 14–17 Years*

| Testicle Absent | 5 Years | | 8 Years | | 11 Years | | 14–17 Years | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % |
| 1957: | (2,174) | | (2,166) | | (2,304) | | (1,716) | |
| Right | 21 | 0·97 | 70 | 3·23 | 58 | 2·52 | 4 | 0·23 |
| Left | 7 | 0·32 | 25 | 1·15 | 23 | 1·00 | 2 | 0·12 |
| Both | 22 | 1·01 | 40 | 1·85 | 44 | 1·91 | 1 | 0·06 |
| Total | 50 | 2·29 | 135 | 6·23 | 125 | 5·42 | 7 | 0·41 |
| 1958: | (2,965) | | (2,038) | | (2,666) | | (2,995) | |
| Right | 13 | 0·44 | 24 | 1·17 | 51 | 1·91 | 4 | 0·13 |
| Left | 7 | 0·24 | 12 | 0·59 | 18 | 0·68 | 3 | 0·10 |
| Both | 14 | 0·47 | 13 | 0·63 | 39 | 1·46 | | |
| Total | 34 | 1·15 | 49 | 2·40 | 108 | 4·05 | 7 | 0·23 |

The figures in parentheses represent the yearly numbers in the various age-groups.

### Discussion

From the figures it is seen that the right testicle is more frequently undescended than the left, and that bilateral undescended testicles are much less common. There is, however, a very marked reduction in the frequency of undescended testicles, both unilateral and bilateral, in the age-groups of 11 years to 14–17 years, thus giving a total proportion of undescended testicles after puberty of 0.41% in 1957 and 0.23% in 1958. This suggests that at the age of puberty most testicles descend without treatment. It is probable that two factors are concerned in explaining the fluctuation of the figures in the 5, 8, and 11-year groups: firstly, the variation in observers, and, secondly, the possibility that retraction may occur more readily in boys of 7–11 years than in 5-year-olds.

It is difficult to explain why the figures should be lower in 1958 than in 1957. Perhaps the experience gained by the observers in the earlier year may have been a factor in the more successful palpation of some retractile testicles.

### Summary

A survey of 19,024 boys at the ages of 5, 8, 11, and 14–17 years was made in 1957 and 1958 to determine the number of unilateral and bilateral undescended testicles.

A marked fall in the percentage of these conditions was found to occur between 11 years and 14–17 years.

It is suggested that hitherto undescended testicles may naturally descend into the scrotum at puberty. If this is true it may produce a reorientation in the approach to treatment.

We thank Dr. R. G. Sprenger, principal school medical officer, who instigated and encouraged us in this investigation, and our colleagues of the School Health Service, Nottingham, for their help in this survey. We also thank

Dr. Sumner, of the department of education, University of Nottingham, for his kind assistance in the preparation of the statistical evidence.

REFERENCES

Coley, W. B. (1919). *Surg. Gynec. Obstet.*, **28**, 452.
McCutcheon, A. B. (1938). *Med. J. Aust.*, **1**, 654.
Scorer, C. G. (1955). *Brit. J. Urol.*, **27**, 374.
—— (1956). *Arch. Dis. Childh.*, **31**, 198.
Smith, R. E. (1941). *Lancet*, **1**, 747.
Society of Medical Officers of Health (1958). *Med. Offr*, **100**, 379.

# A POTENTIAL NEW THERAPY FOR FEBRILE SEIZURES*

## PRELIMINARY REPORT ON DEVELOPMENT OF *N*-PHENYLBARBITONE

BY

J. GORDON MILLICHAP,† M.D., M.R.C.P., D.C.H.

Febrile seizures occur commonly in infants and young children, and generally in response to fever caused by acute infections of the upper respiratory tract. The height of the fever is an important factor in aetiology, and the body temperature at the onset of the convulsion is a reliable measure of the febrile-seizure threshold (Millichap, 1959). Patients with a high threshold convulse only in response to fever of 41° C. (105.8° F.) or above, whereas those who are most susceptible have seizures with fever of 38.5° C. (101.3° F.) or below.

Conventional methods of treatment have been found inadequate. Phenobarbitone, administered intermittently at the time of febrile episodes and in combination with acetylsalicylic acid or continuously in repeated daily doses, failed to prevent recurrence of febrile seizures in 48% of 40 patients treated; phenytoin sodium given regularly and daily was entirely ineffective in seven patients. Tepid water-baths and other methods of hydrotherapy also were unsatisfactory (Millichap, Aledort, and Madsen, 1960).

The ideal therapy for febrile seizures should have both antipyretic and anticonvulsant effects in doses relatively non-toxic. Since seizures occur only at the time of an acute febrile illness, the action of the drug should be rapid in onset and allow intermittent administration so that necessity for continuous medication may be avoided. In the present study a new compound with potential activity against fever-induced seizures has been developed as the result of laboratory tests in animals. Its clinical efficacy has been demonstrated in preliminary trials.

### Methods

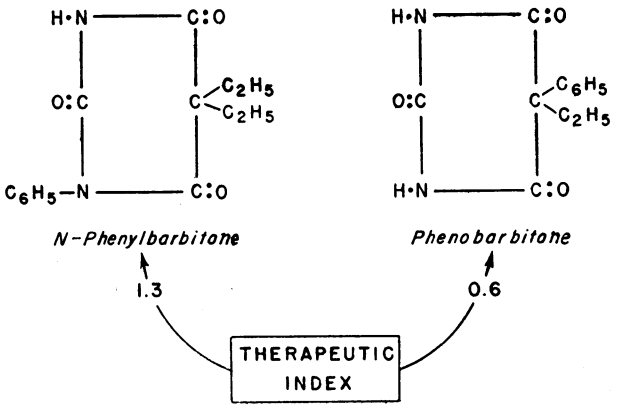
Febrile seizures were induced in young Swiss albino mice by means of a microwave diathermy generator, according to a method described previously (Millichap, 1959). Drugs were tested for their ability (1) to retard the rate of rise of body temperature, (2) to raise the threshold convulsive temperature (temperature at the onset of clonus), and (3) to abolish the seizure. Various doses were employed and between 5 and 10 mice were treated at each dose level. Responses of test animals were compared with those of controls. The effects of acetylsalicylic acid, phenobarbitone, and phenytoin sodium were examined initially so that the efficacy of new drugs could be compared with conventional methods of treatment and their potential clinical value assessed. The selection of new chemicals for testing was facilitated by preliminary observations of the activity of various classes of pharmacological agents against seizures induced experimentally (Millichap, 1958).

### Results

Acetylsalicylic acid in oral doses of 10, 50, and 100 mg./kg. failed to retard the rate of temperature rise in mice and in toxic doses (600 mg./kg.) increased the severity of the febrile seizure. The inadequacy of acetylsalicylic acid in the prevention of febrile seizures may be explained in part by the failure of its antipyretic effect in the presence of a rising temperature. The ineffectiveness of phenytoin sodium against fever-induced seizures in children was observed also in animals; oral doses of 10, 20, and 50 mg./kg. exacerbated the clonic pattern. Phenobarbitone retarded the rate of rise in body temperature and prevented the febrile seizure, but large depressant doses were required; with smaller doses protection from seizures was incomplete but the threshold convulsive temperature was elevated.

Of 60 new chemicals tested, *N*-phenylbarbitone (" pyrictal ") was the most potent anticonvulsant; its action was rapid in onset and toxicity was relatively low. In doses larger than those necessary for control of seizures in mice, hyperexcitability was the principal side-effect and, in contrast to phenobarbitone, sedation was of minimal degree; tremor and clonic movements were observed with sublethal doses of 600 mg./kg. Similar side-effects have been noted in other species, in acute and chronic toxicity studies performed by the Wellcome Research Laboratories, U.S.A. (E. J. deBeer, personal communication).

The chemical structure of *N*-phenylbarbitone and of phenobarbitone and the respective therapeutic indices are as follows:




The therapeutic index is a measure of the margin of safety and potential usefulness of a drug; it is obtained by dividing the dose which causes minimal signs of toxicity in 50% of animals ($TD_{50}$) by that which protects 50% of animals from the experimental seizure ($ED_{50}$).

Laboratory and clinical evaluations of *N*-phenylbarbitone and phenobarbitone are compared in the Table. Determinations of parallelism and estimates of relative potency and toxicity were made by the methods of Litchfield and Wilcoxon (1949). Dose-effect lines of the two drugs were parallel. The potency of anticonvulsant

*Presented at the Ninth International Congress of Paediatrics, Montreal, Canada, July, 1959.

†At present at the Massachusetts General Hospital, Boston, Mass., U.S.A.