test-tube is chilled; under these circumstances an excess of cold antibody causes the red cells to agglutinate almost immediately, whereas a normal amount fails to produce agglutination even after prolonged chilling.

Tests were recorded as positive or negative respectively, and were compared with titrations in 92 instances; they were usually positive at a titre of 64, always negative at 16 or lower, and always positive at 256 or higher.

The diagnostic value of the test was assessed in 583 children and adults suffering from a variety of conditions. With 3 exceptions a rapid screening test was positive only in association with virus pneumonia.

The test has several advantages over titration as a method for estimating cold agglutinins: (1) Venepuncture is unnecessary; (2) no special equipment is required; (3) it is a measure of the avidity of agglutination as well as of the titre; (4) it takes less than a minute to perform; (5) the same sample of blood can be tested as often as desired. It has been found of considerable value in the diagnosis of virus pneumonia and could be performed as readily in general practice as in hospital.

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PRIMIDONE TREATMENT OF ATHETOSIS IN CHILDREN

BY

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Drugs have so far played little part in the treatment of congenital athetosis, and many that appeared promising on paper have proved disappointing in practice. One such drug was benzhexol ("artane"), which was shown to be not only useless but dangerous in a strictly controlled therapeutic trial, using the "double blind" method (Lorber, 1955).

As a result of a statement by Plum (1957) that small doses of primidone had helped 18 out of 31 athetoid children, it was decided to conduct a pilot trial with primidone in a selected group of athetoid children, and to follow this by a full-scale controlled trial if the results justified it.

Material and Methods

For the pilot trial nine patients were selected. All had already attended the out-patient clinic and physiotherapy department for at least four years, so that their abilities and the range of fluctuations in their condition were well known. With one exception all were educable and attended various special schools. Eight were between 6 and 12 years of age and one was a youth of 18. They had a variety of types of athetosis, which in six of them was the result of kernicterus. All had been included in the previous trial with benzhexol.

Primidone ("mysoline") was dispensed as an emulsion. The initial dose was 25 mg. twice daily, and was raised to 75 mg. daily if there was no therapeutic response or evidence of toxicity. The maximum duration of treatment was three months. A placebo, with similar taste and appearance, was then given to those children whose parents considered that improvement had occurred. None of the children had had primidone treatment before the present trial.

The parents were informed that a new drug was to be given to their children and that the drug was known to be helpful in a proportion of children like their own. They were not informed when the drug was changed to a placebo. They were asked to note with particular care any new features, good or bad, during the administration of the drug. At the same time the school-teachers were also informed of the new treatment through the school medical officers and were asked to report on the condition of the children during the trial.

The children were observed for a further period after discontinuation of the drug and placebo.

Results

A full course of three months was completed in eight children. Treatment was interrupted after five days in one hypotonic athetoid child aged 10, because he became so weak and unsteady that he could no longer stand. According to his mother's description "his legs went like jelly." His deterioration was also noted by his school-teacher. On the stopping of treatment he quickly returned to his previous condition. The response of this child to very small doses of benzhexol had been very similar four years earlier.

A second child, aged 6, was a little less steady and became drowsy during treatment. His teacher reported that he was "there in body, but not in spirit" during this period. He, too, regained his previous condition immediately at the end of the course of treatment. Five children showed no response whatever either subjectively or objectively.

Finally, the mothers reported appreciable improvement in two children on primidone treatment. They had more initiative, and attempted tasks with some measure of success which they had never tried before, and became generally steadier. Objectively there was no detectable change in their condition on neurological examination. They were then given a placebo, and they retained this improvement not only while they took a placebo but also subsequently when all drug treatment was discontinued.

Discussion

The results of this pilot study were so disappointing that it was not felt that a trial on a larger scale would be worth while. The doses of primidone were of the same order as those used by Plum (1957). A further increase in the dose was thought to be dangerous in view of the sensitivity of athetoid patients to certain drugs—for example, benzhexol—and of the toxic symptoms observed in two patients during this trial with small doses of primidone.

Summary and Conclusions

Primidone, in doses of 50 to 75 mg. daily, was used in the treatment of nine patients with congenital athetosis. In five no change was detected. Two showed subjective improvement while on the drug, and this improvement was maintained while receiving a placebo and after drug and placebo had been discontinued. In two children there were toxic symptoms: hypotonia and weakness in one and drowsiness in the other. It is concluded that primidone, in the dosage used in this trial, is of no benefit to children with athetosis.

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