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THE USE OF "TRIDIONE" IN PETIT MAL

BY

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"Tridione" was first used at Chalfont Colony for Epileptics in October, 1947. The following is a summary of the cases treated with this drug in the following year, with our conclusions.

As we knew little of the possible toxic effects of tridione the trial was limited to 50 cases, but we feel that these were sufficient to assess the efficacy of the drug. The patients were chosen at random; some suffered from petit mal alone and some from petit mal with grand mal. All cases of petit mal were diagnosed solely on clinical grounds. As tridione is effective only when petit-mal attacks are associated with a cortical dysrhythmia of the wave-and-spike type, it is probable that some of the failures were due to the fact that the patients had a dysrhythmia of a different type. (Electroencephalographs were not available.) The ages of the patients ranged from 10 to 68, and they were mostly females.

Dosage

Each patient began treatment with one capsule (0.03 g.) thrice daily; the dose was to be increased to six capsules daily if no benefit was produced. In only three cases was it necessary to administer the maximum amount. Initially, tridione was given to all cases, whether they suffered from petit mal alone or in combination with grand mal, but it was soon realized that tridione does not control grand mal. Moreover, certain cases who had previously only suffered from petit mal began severe grand-mal attacks when given tridione alone. Two cases went into status epilepticus (with subsequent recovery). We agree with Lennox (1947) when he states that he does not regard the term "anti-convulsant" as correct when applied to tridione in its use in epilepsy. An anti-convulsant such as phenobarbitone and/or epanutin is now given in conjunction with tridione to all cases.

Duration of Treatment

Anxiety about the possible toxic effects of tridione led to withdrawal of the drug too soon in some of the early cases. The continued administration of tridione with an anti-convulsant might have led to improvement in these cases, and we are at present treating some of them in this way. We have so far completely withdrawn the drug in only one patient (quoted below), who has reacted successfully. Lennox states that after the withdrawal of tridione there may be no attacks for 18 months. We gradually reduced the dosage when the fits ceased or became much less frequent. A number of patients whose attacks were considerably reduced with tridione showed an increase in attacks when the drug was discontinued owing to some contraindication.

Immediate Effects

Tridione is beneficial in cases of petit mal, a condition which had previously appeared not to react to any form of treatment. The results with some patients, particularly children, were dramatic. Within a short time of the drug being administered there was complete relief in patients previously having frequent attacks. One typical case illustrates this:

T. F., aged 14 years 10 months. Admitted to Chalfont on April 29, 1943. He had suffered from 10 to 21 minor attacks per month for five and a half years. On Oct. 18, 1947, he was given tridione, one capsule t.d.s. Since that date he had one major attack, in November, 1947, and no epileptic attack of any type since. Prior to having tridione he was described as a "dopy" type of child; at present he is a bright and reliable boy and joins in all games with obvious enjoyment.

Apart from cessation or reduction of frequency of attacks, there has been improvement in behaviour defects and mental capacity in several cases, and the patients have expressed a feeling of general betterment. We have not been able to record improvement by the electroencephalograph, as the apparatus is not available. Lennox utilizes electroencephalography as an indication for reducing the dose of tridione. If his cases have had no petit-mal attacks for three months and the encephalograph is free of wave-and-spike formations, he reduces the dosage by one capsule every two months until none is taken, if the attacks do not return. When reduction or cessation of attacks is not accompanied by an improvement in the patient's mental state, this may be due to insufficient time having elapsed for the mental capacity to be judged. An improved mental state may follow, particularly in children and in cases with a short history.

In our experience the best results have been produced in children. Whether this is due to the age of the patient or the shorter duration of the malady we do not feel in a position to say, though Lennox states that the age is presumably the important factor. Age would appear to be no contraindication to the use of tridione. Our oldest case is a woman of 68, whose history is appended:

K. A., admitted to Chalfont on Nov. 12, 1931, with 27 years' history of epilepsy—all minor attacks. Her annual number of attacks was from 150 to 250. She was first given tridione on Nov. 21, 1947, since when she has had six to seven attacks per month.

In addition to the petit-mal attacks recorded by the attendants, presumably there are a large number which must escape observation.

One other factor in assessing the value of original treatment, particularly in adults, is the patient's suspicion of a new drug; in some cases this resulted in a lack of co-operation and hysterical manifestations.

Toxic Effects

Visual.—There were no serious toxic effects in our cases. Photophobia, or the "glare" phenomenon, particularly when the patient was out-of-doors, has been the most common manifestation, although this has occurred only in adults. There was no evidence of intrinsic eye changes. In no case was it necessary to discontinue treatment on this account, and the condition appeared to occur irrespective of dosage.

Blood.—White cell counts and haemoglobin estimations were done at monthly intervals. We had decided that if the count fell below a total of 4,000 white cells we would stop the drug. This occurred in one case, and the count improved considerably after the tridione had been discontinued. Lennox lays down that a white count of below 4,000, with polymorphonuclears less than 40% or numbering less than 1,600, are indications for at least temporary discontinuance of medication. The haemoglobin remained normal except in one case with a reduction to 60%; there was no evidence that the diminution was due to the tridione.

Skin.—Two children developed a morbilliform eruption, one having in addition a severe stomatitis, presumably due to the drug; the blood picture was normal. The condition cleared up shortly after tridione was discontinued.

Gums.—There was no effect on the gums, such as the hyperplasia that follows epanutin administration.

Ataxia.—There was no case in which tridione could be incriminated.

Indications for Stopping Treatment

These are: (1) an increase in the number of attacks, (2) failure to control petit mal, and (3) manifestation of toxic symptoms. The dose of tridione was increased to six capsules per day, when necessary, before we considered it had failed to control the petit mal. One important factor in the use of tridione is that, unlike the anti-convulsant drugs, it can be withdrawn abruptly without ill effects.

Summary of Cases

Children.—Fourteen cases.

Boys.—Ten cases, aged between 10 years and 14 years 11 months. Attacks have entirely ceased in four cases. In case 1 they ceased in seven months, in case 2 in six weeks, in case 3 in four weeks, and in case 4 in four months. Case 1 was having 100 attacks a month; case 2, 65 attacks a month; case 3, 10 to 20 attacks a month; and case 4, 35 attacks a month. The remaining 10 cases showed from 10% to 90% reduction in the number of attacks.

Girls.—Four cases, aged between 11 years 11 months and 13 years 11 months. Case 1 was exhibiting the akinetic type of attack. She has ceased to fall in the attacks, and they were reduced by about 15%. In cases 2 and 3 the attacks were reduced by 50%. Case 4 had shown a marked reduction in her attacks, but after four months' treatment tridione was withheld when the total white cell count fell to 4,000 per c.mm.

Adults.—Thirty-six cases.

Females.—Twenty-six cases, aged between 16 years 10 months and 68 years. Attacks ceased in six months in one case that was having 120 to 300 attacks a year. Thirteen cases showed a diminution in the number of attacks. Seven cases showed little or no improvement. Three of these cases were among the earliest treated with tridione, and began severe attacks of grand mal as soon as therapy was started. Two of these cases are now receiving tridione again, and doing well. Two cases were apparently worse with tridione.

Males.—Ten cases. Of these, eight cases showed improvement and two no improvement.

From the foregoing it will be seen that in boys 28.5% showed cessation of attacks, and in girls 75% showed improvement. In female adults 3.7% showed cessation, 50% improved, and 7.7% became worse. In male adults 80% showed improvement, and 20% showed no improvement.

We are now giving tridione to more patients. The drug appears to be of use in all cases of petit mal, although it is of little or no value in the treatment of grand mal.

Summary

Conclusions are given of the treatment of 50 cases of petit mal with tridione over one year. Tridione is of value only in the treatment of petit mal. Dosage and toxic effects are discussed.

An analysis is given of the effects of treatment upon adults and children. The best results were with children.

My thanks are due to the committee of the National Society for Epileptics for their permission to publish these results, and to the matron and nursing staff for their co-operation.

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CASE OF *SALMONELLA* ENTERITIDIS SEPTICAEMIA WITH LUNG ABSCESS

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Although *Salmonella enteritidis* (Gaertner's bacillus) infection is usually characterized by an acute gastro-intestinal illness with a pyrexia, many authors report a positive blood culture. Huang (1937) reviewed 50 cases of *Salmonella* septicaemia, most of which also had a coincidental debilitating disease—e.g., relapsing fever. There is a striking similarity between the features of *Salm. enteritidis* septicaemia and typhoid fever.

The usual onset of *Salm. enteritidis* septicaemia is sudden, with fever and generalized aches. A continuous fever with a relative bradycardia often occurs in the second week. A moderate anaemia with a leucopenia is frequently present. An enlarged spleen is almost constant. Rose spots about 3 mm. in diameter, not fading on pressure, are a feature at this stage. The blood cultures are positive in the first two weeks, and the organisms can be recovered from the stools and the urine later. Serum agglutinins are not usually detected until the fourth week.

Occasional variants from this clinical picture have been recorded—e.g., hepatic enlargement. Necropsy findings include hyperplasia of Peyer's patches, haemorrhages in the gastro-intestinal mucosa, and inflammatory lesions of the brain, gall-bladder, bile ducts, and lungs.

Predisposing Factors and Prognosis.—Most authorities stress the importance of malnutrition and debilitating disease, which is emphasized in the case report below. The mortality is high, and due to the frequent occurrence of complications.

Complications

The complications recorded include meningitis, pyelitis, osteomyelitis, cholecystitis, cholangitis, and pulmonary