LETTERS TO THE EDITOR

The Action of Decamethonium Iodide in Birds

SIR,—The mechanism by which neuromuscular block is produced in mammals varies with different substances. Drugs like *d*-tubocurarine chloride act solely on the motor end plate and render it insensitive to the depolarising action of acetylcholine. On the other hand decamethonium iodide can set up propagated contractions when applied sufficiently suddenly (Zaimis[1]) and, in any case, causes a depolarisation which extends to the motor end plate as well as to the muscle fibre (Paton and Vianna Dias[2]); it therefore produces neuromuscular block. Superficially, the paralysis produced in mammals by such an action is indistinguishable from that produced by the curarines. The position however is different when animals are used in which depolarisation of a muscle fibre produces not only electrical inexcitability but, in addition, contracture. This is the case with amphibian and avian muscle, as also with mammalian muscle after denervation. The contracture produced by decamethonium iodide on amphibian and denervated mammalian muscle has been described elsewhere (Paton and Zaimis[3], Zaimis[1]). The present experiments deal with avian muscle.

In adult fowls or chicks, and in pigeons, an intravenous injection of decamethonium iodide was found to cause a rigid extension of the limbs and retraction of the head (see Figure). If the dose is lethal the animal dies in this rigid condition, if the dose is below the lethal level the recovery is abrupt. Decamethonium iodide is highly active, 0·05 mg/kg. causing spasticity for about 3 minutes in chicks. This is a peripheral effect and the shortening of the muscle is probably a true contracture like that described by Langley as produced in the fowl by nicotine. The excitability of the muscle to nerve stimulation was found to be reduced. The full proof naturally requires electrical analysis of the condition. This reaction of avian muscle to decamethonium iodide is a further confirmation that the action is essentially like that of acetylcholine (Zaimis[1]). Tubocurarine chloride on the other hand causes the usual paralysis in birds (see Figure); a dose of 0·5 mg./kg. producing a paralysis that lasts for about 10 to 20 minutes in chicks. Succinoylcholine dibromide, another synthetic substance causing neuromuscular block (Bovet *et al.*[4], Walker[5]), and tetramethylammonium iodide which have both been found to depolarise muscle fibres in a similar way to decamethonium iodide (Paton and Vianna Dias[2]) produce the same spastic conditions when injected intravenously in birds. On the other hand tri-(diethylamino-ethoxy)-benzene triethyl iodide (Bovet *et al.*[6]), now called flaxedil, a synthetic substance, curare-like in most of its actions, causes in birds a paralysis like that of *d*-tubocurarine. From these findings it appears that not only amphibian muscle and denervated mammalian muscle but also avian muscle may be used as a test in differentiating a true "curare-like" blocking action from the superficially similar resultant action of substances like decamethonium iodide. The advantage of using the test on avian muscle is the ease with which the difference in the action of these two groups of drugs can be strikingly illustrated.

We are grateful to Dr. J. Walker for the supply of succinoylcholine dibromide. This work is being done with the aid of a grant from the Medical Research Council.

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November 1, 1949.

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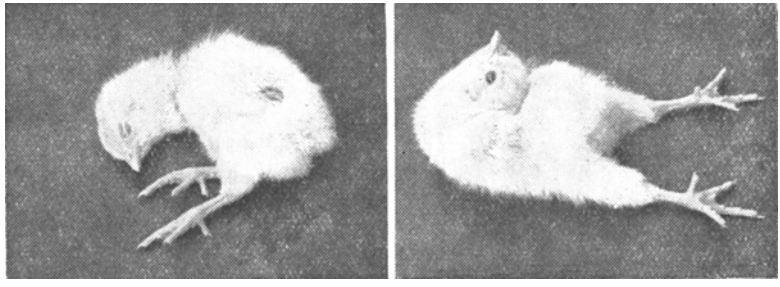

A comparison of the effects of an intravenous injection of decamethonium iodide (right) and *d*-tubocurarine chloride (left).

ABSTRACTS (*continued from page* 990)

excretion usually continuing for 8 to 10 days after the injection. A quantitative balance test was made on two persons and in both about 75 per cent. of the amount injected was recovered. The authors suggest that the balance is excreted in very small amounts (less than 1 mg. daily) over a period of several months after the injection. S. L. W.

Methyl Alcohol and Formic Acid Excretion in Man. A. Lund. (*Acta Pharmacol. Toxicol.*, 1948, **4,** 205.) After intake of small quantities of methyl alcohol (10 to 20 ml.) by human subjects no methyl alcohol was found in the blood in the course of 48 hours, and the concentration of formic acid in the urine was normal (6·5 to 12·8 mg. within 24 hours). Following intake of large amounts of methyl alcohol (50 ml.) this substance could be demonstrated in the blood (25 to 120 mg. per cent.) after 48 hours; formic acid could also be demonstrated in the blood (2·6 to 7·6 mg. per cent.) and in increased amounts in the urine (up to 2050 mg. per cent. within 24 hours). This increased excretion of formic acid after large methyl alcohol intake reaches its maximum in from 1 to 3 days and is characteristic of methyl alcohol poisoning; cases of poisoning with methyl chloride do not show this increase. The author describes 5 fatal cases of methyl alcohol poisoning and gives figures of methyl alcohol and formic acid concentrations in blood and urine. S. L. W.