THE USE OF CURARE WITH CONVULSIVE THERAPY.

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CONVULSION therapy may now be considered to have established a position for itself in psychiatry, and in particular there is now a consensus of opinion that in states of depression occurring in later life it offers a chance of recovery for the patient unrivalled by any other form of therapy. The treatment is associated with a risk of causing compression fractures of the spinal vertebrae, and especially in the age-groups above 60 one is still concerned with the violence of the muscular spasm produced at the treatment. In July, 1939, at the Woodside Hospital we first commenced to study the problem of vertebral fractures complicating convulsion therapy, and also to investigate the general problems involved in rendering the treatment safe for our involutional cases. Our first attempt was with curarine, which we were enabled to give to a few of our patients in the psychiatric department of the Middlesex Hospital owing to the facilities placed at our disposal by the research pharmacological department. We then established—

1. That curarine given intravenously was safe in controlled doses.

2. That it cut down the total muscular spasm, thus appearing to render the treatment more safe.

3. That its use in no way interfered with the therapeutic results of convulsion therapy.

This work was briefly referred to in the literature, but no detailed publication was made, owing to the outbreak of war, and meanwhile other duties appeared to require the attention of those engaged on the research. Six months later, in the U.S.A., a preparation of physiologically standardized curare became available; and through the courtesy of Messrs. E. M. Squibbs & Sons a sample was obtained which eventually found its way to the Middle East, where I was enabled to utilize it on a number of my Service patients. The drug has meanwhile caught the attention of anaesthetists, but its value in psychiatric practice still appears to be underrated.

Curare has an interesting history, and is first mentioned in the writings of the Spanish Conquerors of S. America—especially those who accompanied Quesada on his epic march to Bogota (*circa* 1520). Sir Walter Raleigh appears to have been the first Englishman to mention it, and it was an Englishman, Waterton, who, about 1820, collected the first crude samples. In 1844 Claude Bernard demonstrated its site of action on the myoneural junction, and in 1936 Ranyard West gave it its first clinical trial in cases of tetanus. It was first used in psychiatry in England in July, 1939, and in 1940 the Americans took up its study with characteristic clinical enthusiasm, so that we now have a marketable product. Curare is obtained as an infusion of the bark and roots

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of *Strychnos toxifera*, and is physiologically assayed by comparing its antagonism to acetylcholine on the gastrocnemius of the frog, and also by the head drop induced when injected into a rabbit's ear.

It acts primarily on the motor end-plate of voluntary muscle, where it inhibits the acetylcholine from acting. It is selective in its action, which shows a regular march first on the muscles of the head and neck, and last of all on the intercostal muscles and diaphragm. It has no effect on the circulation or sensory nerves (i.e. the blood pressure is not affected), and death, when it occurs, is due to respiratory paralysis.

Its action is quick and elimination is rapid, and " curarization " probably requires 65–70 per cent. of the lethal dose. The peak effect is achieved by intravenous injection, and all clinical effects have worn off within 20 minutes. No tolerance is acquired, but some pharmacological change evidently lingers on for some 12 hours, as is shown by the dangerous effect if a second dose is administered within this period. The aqueous solution is very stable and may be autoclaved. Prostigmine is a complete and safe antidote, and adrenaline, leptazol (cardiazol) and atropine all modify its action in some degree. Artificial respiration and intubation are clinical antidotes, the latter for the bronchospasm which sometimes occurs when using crude preparations. Its administration results first in a fuzziness of vision, followed by ptosis and nystagmoid movements of the eyes; later there is relaxation and heaviness of the jaws; tightness felt in the throat and a husky voice; generalized heaviness of the body; inability to lift the head; weakness of all muscles; shallow breathing; and lastly accumulation of saliva in the mouth and fauces and severe dyspnoea, leading to death.

Dosage is estimated according to body-weight and the desired effect, and speed of injection is critical. The maximum clinical effect is achieved when the patient finds difficulty in raising his head. Using the preparation marketed as " Intocostrin," this means a dose of 1 c.c. per 40 lb. of body-weight given intravenously over a period of 90 seconds (equivalent to 20 mgm. active material per 40 lb. body-weight).

It has been found that old people require proportionately more of the drug, and it is of the utmost importance never to give more than one dose within 24 hours. Nursing assistance demands that the patient's head be held forward and the jaw supported. The physician must be prepared to perform intubation, artificial respiration and give prostigmine intravenously.

Ideally, one should always place in position a Bragg-Paul respirator, and with this apparatus, together with prostigmine, the treatment becomes 100 per cent. safe in competent hands, seeing that the lethal diaphragmatic effect is the last to appear and the first to disappear; and animal experiments have suggested that even with a lethal dose, artificial respiration maintained for ten minutes tides over the diaphragmatic paralysis, after which the clinical condition becomes one of safety.

Research in America has investigated the use of synthetic substitutes, such as quinine methochloride, and one worker has successfully employed magnesium sulphate intravenously.

It would indeed be a pity if in the present stage of development of the

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therapeutics of convulsion therapy, this drug does not become generally available. In practice 50 per cent of the above dosage in all probability gives an adequate softening of muscular effect.

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