

A SMALL EXPERIMENT IN THE USE OF ACETYLCHOLINE
IN THE TREATMENT OF NEUROSIS.*

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THE purpose of this experiment has been, in the first place, to bring about improvement in certain patients who were responding insufficiently or not at all to psychotherapy, by the use of this drug for which claims have been made that it is of value in the therapy of some anxiety states, such as those characterized by tension; and in the second place to gain by experience an understanding of how much we are justified in expecting from its use. Within the limited series of eleven patients so far treated, results have been sufficiently encouraging to make us wish to continue.

Acetylcholine produces parasympathetic overactivity, and if large doses are used the action of the heart is arrested. In small doses it lowers the blood-pressure by a direct dilator action on the walls of certain peripheral blood-vessels. After atropine, small doses no longer depress the heart or the blood pressure (Wright, 1945). Very rapidly the acetylcholine that has been injected is inactivated by its esterase and the heart action allowed to recommence. Immediately after the injection the patient feels acutely ill, the pulse slows and he coughs and splutters. With larger doses the pulse stops and there is a brief loss of consciousness; and I have learned not to feel undue concern if the patient is pulseless for 25 seconds. The face is usually red and congested during the coughing stage and this is followed by pallor. Within a minute or two all is over and the patient is able to get up and walk away, although some are pale and may feel faint for a short time afterwards.

Professor Lopez-Ibor (1952) says that he has found this drug useful in treating what he calls "biological" or "vital" anxiety states, such as are characterized by restlessness, dread, apprehension, cardiac dysfunction, dizziness and the like. These he considers are not amenable to psychotherapy but can be treated by drugs, while psychotherapy is of supportive value. He considers E.C.T. unsuitable as a remedy for them and favours acetylcholine. Sargent (1952), believes that the ailments most likely to derive benefit from acetylcholine are mildly obsessional states with tension, especially in patients of pyknic or athletic physique, and cases of anxiety with regard to one particular topic.

Case 1 was a man of 48, a telegraph operator, married with no children, who had been anxious for years. Anxiety seemed to be related especially to his work and other symptoms were indecision, fidgeting, obsessional necessity to check things

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over and over again, want of confidence, panics, hiccough after meals and occasional flatulence. After the outlines of his illness had been sketched in a few interviews he was given a course of 22 acetylcholine injections in thirty days. This, however, made no substantial alteration in his condition. He did, indeed, say spontaneously that he thought the medicine had helped him and added, "This four weeks have done me a world of good," but I myself was not impressed. His illness had at first appeared very much the sort that had been described as likely to respond to acetylcholine, but in reality was a hysterical neurosis and therefore unsuitable.

Case 2 was that of a lady, 32 years old, who suffered from an obsessional type of anxiety state characterized by a compulsive need to pick up broken glass, to put straight any accidental damage or to relieve any distress she might discover. She was terrified lest she should see some accident, even a trivial one, about which she could do nothing. If the compulsion were frustrated she would have feelings of tension, dyspnoea or of being "overwhelmed." There was also a considerable element of marital difficulty for which the patient was not primarily responsible. There were no children. Her illness proved to be amenable to psychotherapy and to the social therapy of a neurosis unit, so that after a series of just under 50 psychotherapeutic sessions she has been able to make major adjustments in her domestic situation and is reasonably well and doing a useful job of work. In the middle however, of this treatment I wondered if we could help her to deal with some of her immediate anxiety and feeling of tension, at that time considerable, by a series of acetylcholine injections. Of these, she had ten in fifteen days, and at the end of this time she felt she had been helped by the injections, although she was so terrified by the feelings of acute distress that each induced that she could not allow me to continue the treatment. In this case it seems that acetylcholine was of value in helping to tide the patient over a difficult time, while psychological treatment was still under weigh.

Case 3 is similar to the last in that the main treatment was psychotherapeutic, and in other respects. A married lady of 21 suffered severe distress from a phobia of insects, and in the end a satisfactory result was achieved after a series of 100 psychotherapeutic interviews, even if the case is too recent to allow a cure to be claimed. There came a time, towards the end of the series of interviews, in mid-summer when insects were numerous, when she experienced excessive anxiety and distress, so that I felt forced to seek for some adjuvant. Under these circumstances resort was had to acetylcholine, and this patient received 9 injections in 66 days. Once again the injections had to be stopped on account of the apprehension to which they gave rise; yet they seemed to have done good, and I was sufficiently pleased with this to feel that I would take similar action if similar circumstances were to arise in the case of some other patient.

Case 4.—This was an intelligent young man, aged 28, of good character and pleasant disposition, many of whose symptoms were of a phobic nature. Since the age of 14 he had suffered from bilious attacks. When he came for treatment at the end of 1951 he complained of claustrophobic attacks in crowds, and especially in buses or trains, of sleeping poorly (getting off to sleep all right but waking at 2.30 or 3.0 a.m. and then dozing till morning), and of having been unable to go to work recently because he could not face the travelling. There had been a recent phase, lasting about 3 weeks, in which he said he did not know what to do with himself if left alone, had walked about the house feeling intensely lonely and had cried two or three times a day. He had a periodic sensation of weakness in his limbs, numbness in his palate and other symptoms. It may be that an element of endogenous depression existed here and that E.C.T. would have produced results, but I have a strong reluctance to use E.C.T. until I am sure that it is the treatment of choice, and in this instance I concentrated on a psychotherapeutic approach throughout. From this he gained not a little, but in the middle of it he was feeling "tense and keyed-up," apprehensive and depressed, and I, therefore, gave him a series of 9 acetylcholine injections. These unfortunately enhanced his symptoms and for this reason I discontinued them. This is the only case in which the acetylcholine definitely made the patient temporarily worse. Psychotherapy was continued and a satisfactory result obtained.

Case 5.—This 28-year-old man complained of excessive shyness, which had prevented his forming any attachment to members of the other sex, and also of tinnitus, paraesthesiae of the face, loss of interest in his job, difficulty in getting to sleep at night and mild depression. As a child he was afraid of the dark; in the army he

suffered from headaches and other symptoms ; his present symptoms had existed for several years. A matrix intelligence test gave a low average result ; unfortunately his principal occupational interest was in nuclear physics. On account of his depression he had already been treated by E.C.T. and desoxycorticosterone with little benefit. Psychotherapy appeared unpromising in his case, but he did gain something from the social therapy of our neurosis centre (which had not been opened at the time when he was given the electrical treatment). Here he was given five injections of acetylcholine, but the attempt had to be given up as he was so afraid of the immediate reaction.

Case 6.—A man of 37 complained that during the past year he had been acutely irritable, wanted to cry, wanted to be on his own, felt jumpy inside, was obsessed by fears and by the names of those of his friends who had died, and was absent minded so that he would, for instance, go to make tea but actually do something "silly" instead. He was tense and agitated. He was treated by psychotherapy, E.C.T. and methedrine injections, to none of which he made a good response, and I then decided to try him with a course of injections of acetylcholine. He had only 13 injections but the improvement in his condition was rapid, appreciable and sustained. It is necessary to add that there were one or two features of this case which gave rise to a suspicion of possible underlying psychosis, but they can be disregarded for the present.

Case 7.—This was a 24-year-old, married lady who had a severe claustrophobia, at times amounting to numerous bad panics in the course of one day and giving rise to thoughts of suicide. She had had a good deal of treatment before she came to us and I decided to see what acetylcholine could do for her. She had 12 injections but they did not do the slightest good, and as she was seriously anxious and phobic I resorted to intensive E.C.T., which produced a limited degree of amelioration.

Case 8 was a man aged 39 who had a chronic neurosis, in which he at times felt depressed, and whose wife found him almost impossible to live with. He had been treated in the army by in-patient E.C.T. with short-lived improvement, had come to my clinic a number of times the previous year at his wife's instigation and now came referred by the Ministry of Pensions. In an attitude of experiment—because no known remedy seemed likely to do him much good—I used acetylcholine. He attended as an out-patient for seven injections and then, without giving any reason, he ceased his attendances. (Recently, his wife having left him, he has come to me in a more co-operative frame of mind and there appear to be psychotherapeutic possibilities.)

Case 9 is that of a hysterical, married man of 46 whose insecure personality seemed to provide a poor foundation for psychotherapy. Acetylcholine represented a shot in the dark in the hope of providing a greater degree of inner contentment. The 23 injections he received appeared to have some suggestive value in alleviating his symptoms but no specific effect was noticeable.

Case 10, a lady aged 28, with a known tuberculous lesion of the lung, had been admitted to the neurosis centre with a hysterical type of depression. A nervous breakdown had occurred on Service six years previously, and during the present illness she had already been treated by psychotherapy, including ether abreaction, sedation, modified insulin and E.C.T., to say nothing of the social therapy of the unit, which did produce a little alleviation while its influence operated ; and it was after all this that I decided to give acetylcholine. She had nine injections, some of them producing a severe immediate reaction, but did not improve.

Case 11, is in a somewhat different category from the others, but is of interest because of the lesson his treatment taught me. He was a man of 41 who came for treatment in a state of acute anxiety, but who early showed psychotic symptoms, which I eventually felt justified in regarding as being schizophrenic. Fiamberti (1950) in a lengthy paper has claimed good results from acetylcholine in treating schizophrenics using large doses of 0.5 gm., and he says that in over 50,000 injections he has had no fatalities from the drug. It seemed that the patient in question was the sort who should be likely to benefit and I worked up to this large dose with him. An interesting feature of his case was the occurrence of acute epigastric or precordial pain after each injection, attributed to over-stimulation of the parasympathetic splanchnic nerves. After his 30th injection he began to revive, and then suddenly collapsed so completely that death seemed imminent. He recovered quickly after an intra-cardiac injection of adrenaline. This experience led me to decide that 0.4 gm. should in future be an absolute maximum dosage.

The method I am using is to begin with a dose of 0.06 or 0.08 gm. in about 1 c.c. of water and to inject this *rapidly* into a vein. Subsequently the dosage is stepped up a little each time until perhaps 0.2 gm. is reached. Anything above 0.25 is probably in the realm in which caution is necessary, although some patients easily tolerate more than this, in some cases up to 0.4 gm. I have come to like the minimum dose which will produce unconsciousness. Because of the severe discomfort that some patients feel I have begun to experiment in giving seconal, 1½ gr., beforehand. This has been helpful. but in one case under treatment at present and not included in this paper I have been forced to give pentothal, just sufficient to produce unconsciousness, injecting the acetylcholine from a second syringe immediately afterwards. As antidotes in case of emergency I have on the tray adrenaline, coramine and atropine, and a long needle is included just in case an intra-cardiac injection should be required.

The number of patients in this series is much too small to provide an indication as to what sort of clinical syndrome is likely to benefit from acetylcholine. In Cases 2, 3 and 6 we seemed to have gained something, and this suggests that it is likely to prove its value at least occasionally.

SUMMARY.

It has been claimed that acetylcholine is of value in the treatment of anxiety states, mainly those showing certain characteristics. Of 11 patients thus treated 3 appeared to gain appreciable benefit. Acetylcholine has unpleasant side-effects but these are short-lived, while large doses may be dangerous. The total impression made by this trial is that it will be worth while to continue using this new remedy in selected cases.

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