LEPTAZOL THERAPY IN MENTAL DISORDERS: A MODIFICATION USING SODIUM AMYTAL.

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AT a time when treatment by electrically induced convulsions is attaining a rapid and widespread popularity in clinical psychiatry, it is well to take stock of alternative methods. The purpose of this paper is to describe a method of modifying the treatment of mental disorders by leptazol (cardiazol, metrazol, phrenazol) so as to remove the unpleasantness hitherto associated with this treatment. Though leptazol therapy is still widely employed in psychiatry, its use has, for two reasons, become increasingly restricted. Firstly, it is very unpleasant for the patient; secondly, newer physical treatments, no less empirical, often yield better results in the conditions in which it was used.

In clinical practice it is probable that the first reason has so reduced its popularity that of recent years too little attention has been given to its relative therapeutic merits. If the treatment can be rendered acceptable to the patient, it becomes pertinent to ask if and when it is indicated. There are three possibilities:

(1) Cases in which it is the treatment of choice.

(2) Disorders which have recently failed to improve with other empirical methods, and which often do improve with a course of leptazol; or disorders in which the treatment of choice is contraindicated on coincidental grounds.

(3) Miscellaneous circumstances, such as patients who refuse electrically produced convulsions; situations in which the apparatus for these is not available; or others mentioned below.

It has been advocated as the treatment of choice in catatonic stupors and certain schizophrenic reaction-types refusing food. It has been recommended in some hysterical syndromes with depressive features; in the excitement of mania; and in illnesses characterized by symptoms of self-depreciation and inferiority, or depression with expressed feelings of unworthiness or guilt. Many psychiatrists favour it in various affective disorders, opinions differing as to those in which it is most effective. I have found it very successful in an acute syndrome in young men, possibly seen more often during the war years. It superficially resembles early schizophrenia simplex, but the breakdown seems reactive rather than endogenous; it occurs in a personality previously healthy or perhaps rather inadequate, but not truly schizoid; and the subject

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is dominated by ideas of inadequacy, hopelessness or uselessness in society, inferiority, self-depreciation, unworthiness or real guilt. It is the mental trend and content which is predominantly disturbed. Five of my cases were of this type and they responded well.

Other psychiatrists, though not accepting that it should be used first in the above conditions, will agree that in many of them it produces an improvement sufficiently often to make it indicated when other treatments have failed. This provides a large number of cases under Group 2.

Group 3, though not a psychiatric classification, is at the same time much less a matter of personal opinion and cases in this group are not uncommon. I have had two men who refused electrically produced convulsions and would have gone to any length to avoid them because they had seen the fits produced by the apparatus when patients were treated *en masse*. There are other patients who are horrified at being connected to mysterious electrical apparatus, but who fairly readily agree to an injection. Such patients would probably also object to leptazol injections if the usual unpleasant concomitants of these had to be endured ; but with the method below, they do not. Other patients in this group are those in whom it is important not to impair their memory ; and early schizophrenic reactions, encountered at the out-patient clinic, who will not, or cannot for domestic reasons, consent immediately to a long course of insulin therapy or any treatment necessitating hospitalization.

The Problem.

There are, then, in the present state of our knowledge, definite indications for leptazol therapy. If it could be made palatable to the patient it might be held much more in favour. Reasoning from the fact that in electrical convulsion therapy it is presumably the retrograde amnesia which renders it acceptable to most patients, I sought to produce such an amnesia in leptazol therapy, particularly for the terrifying experiences, cumulative in effect, which occur between the injection and the convulsion, experiences sometimes referred to as the aura. Starting with feelings of apprehension, strangeness or unreality, it progresses to sensations of choking, buzzing and tingling ; unpleasant olfactory, gustatory or vivid visual hallucinations ; fantasy formations ; and, finally, stark terror. The intense struggling and pleading exhibited to avoid this are familiar phenomena. Cook has stated the problem in a paper in which he discusses the role of fear in leptazol convulsion therapy. He remarks that even partial amnesia helps to allay subsequent apprehension, and that a complete amnesia, sufficiently retrograde to include the preparatory phases, should go far to remove one of the greatest drawbacks of the therapy. I feel certain that the whole objection to treatment is due to fear of the aura period, and other writers entirely agree with this. Attempts have been made to dull the patient's perception of the aura by hyoscine hydrobromide, or paraldehyde premedication, induction of insulin hypoglycaemia, administration of nitrous oxide to the point of asphyxia—all of course before the injection of leptazol.

I have experimented with soluble hexobarbitone prior to the leptazol, the aim being to inject this slowly until the patient is practically unconscious ; to

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wait until he has partly revived; and then to inject the leptazol. Briefly, as hexobarbitone is antagonistic to leptazol, it is not practicable to choose a dose which is large enough effectively to narcotize the subject and yet not large enough to impair the action of leptazol. A small dose of soluble hexobarbitone merely dulls the patient's perception, so that his memories are rather less vivid, but still present; and I abandoned the idea of prior administration of this or any other drug.

Technique.

The method I have adopted is to follow the leptazol convulsion by an intravenous injection of sodium amytal so as to keep the patient fairly deeply unconscious after the convulsion; and in such amount that he remains unconscious for a further half to one hour. There are three simple points to observe:

(1) The time of injection: the sodium amytal is injected immediately respiration becomes regular.

(2) The site of injection: the vein to be used should be selected and prepared before giving the leptazol.

(3) The amount at first injection: it is important to avoid subconvulsive doses of leptazol.

The sodium amytal is not injected immediately after the convulsion, but as soon as respiration becomes regular, usually about 20 seconds later. I have considered it unwise to give an intravenous barbiturate like sodium amytal while respiration is disordered; but there must be no delay when it recovers, for I have found that, if there is, the retrograde amnesia is less complete. Similarly, a subconvulsive dose of leptazol should be avoided, for whether this is followed by a larger dose in order to produce a convulsion, or by the sodium amytal when it becomes apparent that no convulsion will occur, then, in either case the sequence of convulsion—immediate deep coma—light coma, is broken, and there is less likelihood of success. With the sodium amytal the restlessness or struggling which often occur in the minutes soon after the convulsion are completely avoided. After this restlessness the patient does often sleep for a while; but with the sodium amytal the sequence is altered, and the deepest unconsciousness follows the convulsion.

Pre-selection of the site becomes important in patients with bad veins, and in them it may be vital. In such subjects, if only one inadequate vein is found, it is often spoiled by the leptazol and delay in searching for another after the convulsion may lead to failure of the technique. For similar reasons I have a spare syringe already filled with sodium amytal. I also have at hand a syringeful of soluble hexobarbitone ready to inject in cases where a convulsion is not produced. I chose this drug for this purpose because it is more rapid and the amount necessary to get the patient fairly deep is easily judged while the injection is made.

As to the choice of barbiturate for the standard technique, the criterion is that it has the appropriate rapidity of action and of clearance. I have no grounds for believing there can be anything specific about sodium amytal. It has the desirable initial action, and a rate of clearance which from one treatment to the next allows judgment of a dose which will secure the right period of

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unconsciousness. The method has been used on out-patients, where it is convenient to have control over the length of unconsciousness.

The dose is adjusted from session to session. After the first injection of leptazol, in a normal adult I used 0·35 gm. sodium amytal. If the patient remained unconscious for much over an hour I reduced it to 0·2 gm. next time. If he could be roused after only a few minutes, I increased the dose next time, up to 0·4 gm. or 0·5 gm. I tended to use a large dose at the first session, as I did also with leptazol, and later to reduce it, rather than the reverse. In this technique, initial success contributes largely to success over the whole course. In two patients who were difficult to rouse after only 0·15 gm. sodium amytal at the third session, I substituted 0·2 gm. soluble hexobarbitone at the fourth session and adjusted this at subsequent sessions to get the desired result.

Further Modification.

I may mention here a recent further modification with an intravenous barbiturate, not before each leptazol injection, but before the whole course of treatment. At the first session the patient is prepared exactly as he will be at subsequent sessions. He is told he is to have an injection which will make him lose consciousness, and as this suggestion is being made he is given 0·4 gm. soluble hexobarbitone intravenously, or a little more if necessary, and allowed to lie until he wakes. At the second attendance he is given 6 to 7 c.c. of "Injection of Leptazol" and is reminded that he will rapidly lose consciousness; this is followed up by sodium amytal and the course continued as above. I have found the suggestive reinforcement of the first "treatment" is effective, and by the third session the patient is accustomed to the procedure and content in the belief that he is having some sort of sleep therapy. I think this further refinement will give optimum effectiveness to the whole technique.

Results.

In all, 34 in-patients and 16 out-patients were treated and I will discuss them in three groups:

	Group 1.	Group 2.	Group 3.	Total.
In-patients	4	22	8	34
Out-patients	6	9	1	16

The first group, 4 in-patients and 6 out-patients, had what can be called an amnesia for treatment. By this I mean a retrograde amnesia comparable with that obtaining in a patient having electrical convulsion therapy who cannot remember the nature of the previous treatment. It does not imply amnesia for the entire procedure of coming up and having treatment.

In the second group, of 22 in-patients and 9 out-patients, there was amnesia for leptazol symptoms. Though the patient remembered his preparation and the injection itself, he did not remember what followed the injection or did not associate it with anything unpleasant.

The third group had a partial amnesia. They remembered enough of the unpleasantness of the leptazol symptoms to make them dislike further treat-

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ment; but they certainly did not suffer the extreme fear which results from leptazol by itself, and only persuasion was necessary to induce them to continue. Relatively more in-patients were placed in this group because a few could not be regarded as perfectly reliable witnesses; and if there was any doubt they were placed in this group rather than the one above. There was one in-patient in whom we could not be sure that the technique had made any difference.

In no case was there any trace of the restlessness and excitement which sometimes occurs after treatment with unmodified leptazol. Even in Group 3 there were no signs of any of the reactions which may occur in patients recovering from a leptazol convulsion.

The patients were seen after treatment by another member of the medical staff, and we have judged the results from the descriptions and introspection of the patients, on the one hand, and from their reactions to the treatment and to the prospect of more, on the other. Of great assistance was the fact that twelve in-patients had had a previous course of electrical convulsion therapy and four a course of unmodified leptazol; while eight out-patients had had a previous course of electrical convulsion therapy. This provided the background with a measure by which to assess the effectiveness of the present technique. Some patients preferred the course of injections to electrical treatment. In most cases the same sister or charge nurse assisted at both courses and considerable weight was given to their opinion on the reactions of the patients, and especially on what the patients told them about it in the absence of the doctor. In fact, up to the third treatment of each course, I judged the results largely on detailed information obtained from a reliable nurse.

Discussion.

Interesting points emerge from consideration of the patients who actually preferred this treatment to treatment by electrically produced convulsions. I am sure that the preference does not result from an amnesia which in every case was better than that obtaining in electrical convulsion therapy in the average patient. Other factors must be responsible. Now many patients, especially if unaccustomed to the hospital atmosphere or to complicated apparatus, are frightened by the arrangement for electrical convulsion therapy and by the way in which they are prepared for it. If then in leptazol therapy an amnesia can be produced comparable with that in electrical convulsion therapy, so that the patient comes to each individual treatment with the same preconception of it, it is not surprising that many will prefer the more familiar procedure of injection to that of having their head scrubbed, tightly strapped and connected to elaborate electrical equipment. Patients, of all grades of intelligence, know that there is something more in the "electrical treatment" than they have been told.

I suggest that the technique does not necessarily result in a retrograde amnesia as good as that in electrical convulsion therapy; but it does result in one which removes the unpleasant concomitants of leptazol injections. From the figures above it can be seen that 20 per cent. of subjects had an amnesia as good as, or better than, that obtaining with the electrical method. However,

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a further 62 per cent., making a total of 82 per cent., could not associate the treatment with any unpleasant sensations. This is all that was aimed at, but the end-results, for reasons advanced above, are better than anticipated. In the remaining cases the aura phase was reduced by varying amounts. Whatever the mechanism, the treatment is rendered acceptable to most patients.

Further, there is more perfect control, from session to session, in a method involving injections of known amounts of a standard solution. In the electrical method, any one voltage and time setting may not produce the result expected by reference to the previous session; and most clinicians are familiar with the growing apprehension of the patient while technical adjustments are being made.

It is also likely that this modification will lead to better therapeutic results. It has been shown by Cohen, for example, that a large element of fear in leptazol therapy considerably reduces its curative effect; and this technique should enhance the therapeutic value of the method.

Summary.

There are several indications in psychiatry for leptazol therapy, but it has fallen out of favour largely because of its very unpleasant concomitants. A method of overcoming these is described, and its results in a series of in-patients and of out-patients are discussed.

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