SIX MONTHS' EXPERIENCE WITH CARDIAZOL THERAPY.*

By G. S. NIGHTINGALE, M.R.C.S., L.R.C.P., D.P.M.,
Assistant Medical Officer, Brentwood Mental Hospital.

THIS paper is an attempt to record the experience gained in treating 44 schizophrenics in this hospital with cardiazol from September, 1937, when the treatment was first used, to the middle of April, 1938.

SELECTION OF CASES.

The cases selected for treatment may be divided into two main groups: Firstly, recent admissions; of these a large proportion arrive at the hospital suffering from acidosis and from various degrees of auto-intoxication. Glucose and insulin, colonic lavage, and often one of the sulphonamide preparations are first used to improve their general health; then, subject to rigorous physical examination to exclude cardiac, renal or other disease, they are submitted to a course of injections.

Secondly, cases in the chronic wards; from those patients, admitted prior to the use of cardiazol, we have selected for the most part stuporose cases, of any duration, as these appear most likely to benefit from the treatment; also those patients who require feeding, whose habits are degraded, or who exhibit other antisocial behaviour, in whom it seems possible to produce some improvement, however far short of recovery. In practice, some of the latter group have shown surprisingly good results. Finally, preference has been shown to young patients with good family histories, although a certain number of cases of long duration have been treated as "test cases", and of these, two patients with histories of eight and ten years' duration have shown decided improvement. In the more crowded chronic wards the difficulty has been, not so much to find cases likely to derive benefit from the treatment, as to make a final selection from the many possibilities.

TECHNIQUE EMPLOYED.

Until January ampoules of cardiazol containing 3 c.c. were used, but since then the solution has been made up by the hospital pharmacist in rubber-capped vials of 25 c.c. capacity, at the strength of 0·1 grm. per millilitre of

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freshly re-distilled water, with 0·001 grm. di-sodium phosphate added, as advised by the makers. As ordinary rubber affects the pH of a solution, caps made specially to reduce this undesirable effect by Messrs. Britton, Malcolm & Waymark are used.

Tests on the freshly prepared solution give a reading of pH 7·8 ; after one week, that is, twice as long as the solution is normally kept, it had only dropped to pH 7·7. These figures are slightly lower that that of the ampoule solution (pH 8·5), but the clinical results have in no way differed from those obtained when the ampoules were used.

The vials are sterilized in an autoclave for half an hour at 105° C., and are issued to the wards twice weekly containing the quantity of cardiazol estimated as necessary for the particular patients under treatment. It is, however, not possible to give a precise forecast of the amount likely to be used, as there is a day-to-day variation in the needs of individual patients, and allowance has to be made for extra injections should the first be abortive.

The advantages of this method are twofold ; first it has reduced wastage from 20% to below 15%, but recent correspondence with the makers indicates that, where proper care is taken in the preparation and sterilization of the cardiazol, there is no reason why batches should not be made up at weekly or fortnightly intervals, to be issued to the wards as required, provided that, once started, an individual vial is finished within a few days. By this means it is hoped to reduce waste to below 5%. Secondly, it has resulted in an appreciable saving in cost. At hospital prices the cost of cardiazol in ampoules is $3\frac{1}{4}d.$ per c.c. Allowing generously for caps, breakage of vials, heat for sterilizing and all other incidentals, the cost of the home-prepared solution works out at 1*d.* per c.c. At an average weekly consumption of 600 c.c., this equals a saving of £5 15*s.* per week, or £300 per year. Against this must be put the time, two hours, taken to prepare each batch.

A new type of vial is now available, made by the same firm, having a ground neck over which the rubber cap fits without wiring, and which has a screwed bakelite cap.

The use of this type, by obviating the necessity of wiring on and removing the rubber caps, should show a saving of about twenty minutes at each bi-weekly preparation.

The injections are carried out throughout the hospital by the various medical officers on their own cases, and are given to each patient twice weekly, with the patient in a single room, where this is possible, and when two or more cases are treated on the same day, they are separated from sight and hearing of one another, as a noisy patient may upset the others.

The patient, having been given an aperient the night before, or an enema in the morning, and nothing beyond a cup of tea by mouth to reduce the tendency to vomit after the fit, remains in bed till the doctor arrives. It is usual to give the injection into the same arm on each occasion, reserving the other for use should thrombosis occur.

The doctor fills his syringe, which is fitted with a wide-bore needle, outside the room, and gives the injection to the patient without delay. Two nurses only are in attendance, the one to apply the tourniquet and the other to manipulate the gag. Other nurses are in readiness should the patient be violent, but it has been found that ostentatious preparations and a " show of force " increase the patient's apprehension.

The gags used are either of a bifurcated shape, designed to fit the molars, or a plain, covered wooden wedge ; of the former type two sizes are in use, it

being preferable to use as large a size as possible to avoid damage to the incisors.

After the fit the doctor remains until the patient is breathing regularly and has regained a normal colour. The patient is left in bed for several hours, the actual time necessary varying with the individual patient. A nurse remains by the bed for at least ten minutes after the doctor has left, and thereafter, one nurse to three patients has been found to be sufficient observation.

In six very apprehensive patients morphine and hyoscine pre-medication has been used; also in two cases where the patient was so violent that injection was impossible without its use.

On the days when no treatment is given the patients are allowed up, and are encouraged to employ themselves with the various forms of therapeutic occupation and physical training.

The earlier cases were given 3 c.c. as initial and subsequent doses, but this resulted in many "missed" fits; latterly cases have been started on 5 or 6 c.c., and the dose increased as necessary, with better results, the average dose being about 7 c.c. The after-effects of large doses up to 9 c.c. have not been found to be worse than those following injections of 3 c.c. The largest single dose given has been 10 c.c.

The actual speed with which the cardiazol is injected into the vein undoubtedly has a direct bearing on the production of a fit; too much force, however, may rupture the vessel, not only resulting in an extravenous injection and no fit, but also making subsequent injections into the same site difficult; none the less, several cases have had between 25 and 30 successful injections, and one patient as many as 33.

Over 75% of the cases have, on one or more occasions, failed to have a fit following an injection. In many instances this was attributable to too small a dose, or to too slow an injection, or to the cardiazol having been given extravenously. In others, despite rapid intravenous injection and adequate dosage, unexplained failures have occurred. It is now the practice, when a patient has an injection with no following fit, for whatever reason, to give immediately another injection, larger by 1 c.c. than that producing no result. This double-dosage method has not given rise to any untoward effects, except in one instance, where it was followed an hour later by a strong secondary fit and considerable collapse.

Complications.

In the cases under review certain complications have manifested themselves, the most prevalent being a subjective feeling of apprehension, with the objective signs of fear, ranging from the moderate to violent active resistance to the treatment. This apprehension has appeared at some time or another in 62% of the cases. At first it was thought that this was produced by abortive

injections, but a closer scrutiny of the case-records does not reveal a direct relationship between the occurrence of missed fits and the incidence of this apprehension, for it is found that out of 10 patients who have had a fit following every injection, 4 exhibited extreme anxiety, while 10 other patients who have missed as many as six or seven fits each have never shown any fear of the treatment. Indeed, if the patients' personal descriptions be believed, it is hardly surprising that this anxiety should be so frequently shown, for they describe varying but universally unpleasant sensations following the injections, ranging from a feeling of impending death to mere headache and visual hallucinations.

None the less a large proportion actually look forward to the treatment because they " seem clearer in the head " or " feel a lot better ", although they acknowledge an uncontrollable fear of the sensations following the actual injection. One man described the result of his treatment as being " like coming out of an anæsthetic ".

Pre-medication with morphia and hyoscine has not been successful in relieving this apprehension, and in a few cases treatment has had to be stopped because of the patient's violent resistiveness.

In only one case has a fracture due to muscular action during a fit occurred, and this man, who fractured a femur, was pronounced by the visiting surgeon, after X-ray examination, to have early Paget's disease. Two other cases became hypomaniacal and sustained Colles's fractures while employed in ward work, necessitating cessation of treatment.

The occurrence of this aimless excitability has been rather a troublesome feature in the course of treatment, and a number of previously lethargic patients have become extremely mischievous and interfering. In some cases this has been a passing phase, but in others, despite prolongation of treatment, this behaviour change has persisted.

The classical dislocation of the jaw has, so far, not occurred.

Three patients have broken incisor teeth due to the slipping of the gag, but this has not occurred where the wider bifurcated gag has been used.

One female patient on several occasions stopped breathing for so long after the clonic stage that artificial respiration had to be resorted to.

Abnormalities of the fits have occurred in 5 cases; one patient had a succession of three fits following an injection of 5 c.c.; another showed the unusually long latent period of 10 minutes between the injection and the fit, despite normal intravenous injection. This being one of the earlier cases, no second injection was given, and it is possible that, were this not now the practice, the incidence of this delay—presumably one of absorption—might be more frequent. Finally, three cases have had secondary fits 8 hours, 3 hours and 1 hour respectively after the induced fit (the latter case being that already mentioned as having followed a second injection). These two last complications emphasize the importance of close observation for some hours.

A few cases of a mild dermatitis of an eczematous nature at the site of injection have occurred where the cardiazol has been accidentally given extravenously.

Results.

It would be a presumption to base any conclusions as to the permanent value of the treatment on so small and so incomplete a series of cases, particularly as the criterion of completion is largely a matter of personal opinion.

In practice the reasons for discontinuing treatment in the 21 completed cases may be summarized as follows: Three patients have been discharged; these have remained at home for five, four and three months respectively, and the social worker reports them as being well, interested in their occupations and mixing with their friends; the first girl is learning shorthand and typing, the second is employed in a shop, and the third works at home. The latter says she "is proud to have received the 'new' treatment", and volunteered the statement that she thought others who were not willing to have it were foolish. One has regained normality and is awaiting discharge. Two were stopped on account of fractures; 4 as being too violent to continue; 2 proved to be mentally defective after removal of their schizophrenic characteristics; the others, because they have had twenty-five injections and upwards, and were showing no further improvement; 3 of these have since relapsed.

In grouping the types of symptom-complexes as far as possible, and using Kraepelin's classification, which is admittedly of a somewhat arbitrary nature, but which has been used for lack of a better, we find that the katatonic group show the most favourable results. Of the 21 completed cases and 23 still under treatment, 15 come under this heading, of whom 2 have been discharged, 9 are much improved and 2 are socially improved in that they now converse, occupy themselves in the hospital and need little attention. Only 2 cases show no change, 1 of whom only had four injections before sustaining a fracture.

The *hebephrenics* give the following figures: Of the 10 cases, 2 are discharged or pending, 5 are improved, 1 socially improved and 2 show no change.

Of the *simple* type, 6 are improved, 6 slightly better and 5 are unchanged.

Only 2 cases of dementia paranoides have been treated, of whom the one is slightly better and the other unchanged.

As might be expected, those cases with the shorter histories, especially those under one year, show the more favourable results, as also do the younger patients. Of 18 cases with histories up to one year, 4 are discharged, 9 improved, 4 socially improved and 1 unchanged. In the 1–3-year and over 3-year groups the figures are identical, viz., 6 improved, 3 slightly improved, 4 unchanged, in each group.

All four discharged cases are under 20 years of age.

These results are summarized in the subjoined tables:

TABLE I.

	Katatonic.	Simple.	Hebephrenic.	Dementia paranoides.
Total cases	15	17	10	2
Discharged or pending	2	0	2	0
Improved	9	6	5	0
Social improvement	2	6	1	1
Unchanged	2	5	2	1

TABLE II.—*Length of History.*

	Up to 1 year.	1–3 years.	Over 3 years.
Total cases	18	13	13
Discharged or pending	4	0	0
Improved	9	6	6
Social improvement	4	3	3
Unchanged	1	4	4

TABLE III.—*Age-Groups.*

	16–20.	21–30.	Over 30.
Total cases	9	20	15
Discharged or pending	4	0	0
Improved	3	9	9
Social improvement	1	6	3
Unchanged	0	5	3

It has not been found that those patients reacting to the smaller doses necessarily show the better results.

A considerable number have temporary relapses during the course of treatment, particularly where there have been a succession of abortive injections, but the majority improve again later in the course; relapses have also been noticed in those cases where injections have had to be suspended for intercurrent diseases. One girl in particular remains very well as long as she is having the injections, but relapses to a state of mutism a few days after they are stopped, although she has had no fewer than thirty-three fits. A period of several days' comparative normality can, however, usually be produced by giving a single further injection.

It is possible, therefore, that occasional maintenance doses may be needed, even in successfully treated cases.

In a few patients who have improved in that their schizophrenic characteristics have disappeared, there is left an evident basis of mental defect.

Given suitable home conditions, this class of patient might well be discharged from hospital after treatment.

It is interesting to note that one girl who had two courses of fourteen days' prolonged narcosis with somnifaine, without effect, began to improve from the third cardiazol injection, and has not, so far, relapsed.

In conclusion, it would appear from this series that treatment should not be confined solely to those cases with the most favourable prognostic indications, since even the more advanced schizophrenics with histories of many years' duration are capable of some degree of amelioration, with resultant lessening of nursing supervision and improvement in their institutional usefulness.

Finally, I have to thank Dr. Masefield, Medical Superintendent of Brentwood Mental Hospital, for his assistance, Drs. O'Byrne, Morton, Copeland and Tredgold for allowing me to quote from cases under their care, and Mr. Wicks, the pharmacist, for having supplied me with pharmaceutical details.