Clinical Note.

AZOMAN (TRIAZOL 156) AS A CONVULSANT.

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(Received March 26, 1939.)

SINCE Meduna in 1934 introduced the treatment of schizophrenic states by induced epileptiform convulsions, a volume of literature has appeared on the use of cardiazol as convulsant. But although cardiazol proved immensely superior to the original camphor, it is not without some serious disadvantages. These led naturally to the search for further improvement in the convulsant agent, and it is with one of the successors to cardiazol, introduced by Walk and Mayer-Gross (1938), and known as azoman or triazol 156, that this record is concerned.

Azoman was first used in this hospital in October, 1938. Thirty-seven patients have been subjected to convulsions with this agent, and a total of 695 convulsions have been induced. Age-limits in this series have been 18 to 57 years. Although the first development of convulsion therapy was directed against the schizophrenic psychoses, a wider experimental use naturally followed, and Cook and Ogden record the successful application of this treatment to a number and variety of non-schizophrenic states. Azoman has therefore been used in this series to demonstrate that it replaces cardiazol satisfactorily in other than the schizophrenic psychoses. The outcome is the conclusion that azoman is an improvement on cardiazol in all psychoses in which convulsion therapy is of value.

SELECTION OF CASES.

As has been said, selection is no longer limited to the young schizophrenic. Moreover, familiarity has bred confidence if not temerity, the essential similarity between the cardiazol or azoman convulsion and its idiopathic epileptic equivalent has been realized, and the conclusion drawn and confirmed by records that the one need be little more lethal than the other. Though therefore in this hospital as elsewhere risk is not unnecessarily courted, and the prospective patient is required to satisfy a careful general examination with a complete blood picture, the age field has been widely extended, and patients of up to 57 years old have been treated without cause for anxiety on this score. Anyone who has familiarity with the typical mental hospital population knows that apart from the comparatively rare *status epilepticus*, epilepsy *per se* does not usually constitute a risk to life, even in advanced years. It is true that reversible psychotic reactions are less likely to be found in advanced years, and where even the hospital remission, as it has been called, may be hoped for there is justification in undertaking convulsion therapy.

TECHNIQUE.

Azoman is supplied in ampoules of about 2·2 c.c. of a 5% solution. It may be administered orally or by any of the parenteral routes, although the convenience of the intravenous, or at the worst, intramuscular route displaces the need for other approaches. As would be expected, the dose varies according to the route used, being less if injected intravenously and greater orally. Fairly wide individual variation is found, and so gauged in the first place by the usual criteria of age, body-weight and sex, while as far as the two principal routes are concerned, the intramuscular dose is approximately double the intravenous dose. While there seems to be little risk in an initial overdose, the results are likely to be alarming, a condition resembling *status epilepticus* being produced; and it is therefore advisable to start with a dosage of not more than 1 c.c. intravenously or 2 c.c. intramuscularly. This can then be modified subsequently according to the results. But it is reassuring to find that even where, as in four of our own earliest cases, overdosage resulted in a series of convulsions, these can be controlled by the usual methods; light chloroform anæsthesia on one occasion and intravenous evipan on another successfully brought the series to an end, while the remaining two cases were allowed to end spontaneously with no ill-effect.

The interval after the injection before the convulsion occurs depends on the route and dosage, but is rarely less than about 30 seconds by the intravenous route. Where a minimal dosage has been used this may extend to 2–3 minutes. By the intramuscular route the interval may be from 10–20 minutes. Recognition of these limits is necessary in order to judge the point at which supplementary dosage is called for when no convulsion has occurred. Further help in assessing this interval and the necessary supplement is given by observation of the preconvulsive phenomena, which may vary from a few myoclonic contractions up to a violent succession of contractions just falling short of the tonic stage. But the supplement, it should be emphasized, is not, as with cardiazol, the same amount as the original dose. No more than one-half of this amount should be given, and frequently less will be found to be adequate. This applies both to the intramuscular and intravenous routes. Subsequent dosage is then based on the resultant, so that where multiple fits or a particularly vigorous one are produced by the initial or combined dosage, a suitable reduction can be made on the next occasion. This can be followed until the subminimal dose is found, and increase to the minimal dose then provides a fairly constant individual dosage. One of the attractive features of azoman as compared with cardiazol is this close relationship between variation in dosage and variation in results, so that a reduction of ·2 c.c. may fail to produce a convulsion, while a similar excess may be followed by a fit which seems unnecessarily vigorous. Continued observation of this treatment leads almost inevitably to the conclusion that the fractures which are occasionally recorded are most likely to be avoided when the convulsive threshold is not greatly exceeded.

Tolerance has been observed, but does not seem to be the rule. In this series tolerance has been assessed by the relationship between the initial and final dosage; and on this basis 15 patients received a higher final dosage as against 22 who did not. There may, however, be a variation from time to time, small in extent. It is not always easy to be sure that a small quantity of the injections has not been extravenous, and since so small an amount as ·2 c.c. may be significant, such an increase may be made on the following few occasions before it is realized to be unnecessary. In this connection it is worth remarking that there is much less likelihood of extravenous injection where so small a bulk has to be injected, and where the speed of injection is not a matter of consequence. The same factor governs ease of access. Anyone who has had experience of cardiazol is familiar with the difficulty which occurs when sclerosis reduces the number of available veins. And as the major veins become sclerosed, the minor vessels are yet more easily occluded by the size of the injection and the speed at which it is given. Azoman, however, seems to

exert a minimal sclerosing effect, and care of veins becomes a matter of little importance. The small bulk, moreover, which may be given as slowly as is necessary, makes available on occasion the veins on the dorsum of the hand; even hypodermic needles may be used, and the intravenous route therefore rarely presents difficulty. It may be mentioned in passing that the simplest final dressing of the puncture after momentary local pressure is a dab of collodion. Strapping has now been abandoned because of the number of occasions on which a mild antecubital dermatitis has aroused fear of the infected skin through which a needle might subsequently have to be passed. Bandaging is cumbrous, and the collodion seal does least to suggest the idea of trauma to the patient.

Complications.

1. *Fractures.*—These are rare, and unless associated with excessive dosage, resulting in a too violent convulsion or with a patient unfitted for the treatment, unpredictable. Two have been encountered in this series; one was recorded by McGuinness (1939), and the second, a vertebral crush fracture, resembled that recorded by Stalker (1938). None was met with in the previous series of 48 patients subjected to cardiazol.

2. *Dislocation.*—Most writers have referred to dislocation of the jaw, and this has been encountered here also, but it is now no longer allowed to occur, as it has been found that support of the jaw at the beginning of the tonic phase can prevent the hyper-extension which leads to the dislocation. Since this was observed no further cases have occurred. One dislocation of the shoulder occurred.

3. *Vomiting.*—Mayer-Gross and Walk referred to this complication of azoman, but in the present series it has been far from a constant accompaniment. It has generally followed the first convulsion. As a rule it has not continued with subsequent injections. When it has occurred it has been effectively controlled with atropine gr. $\frac{1}{120}$ hypodermically half-an-hour beforehand.

No other complication of note has been encountered.

Sedatives.

It is one of the most outstanding characteristics of azoman that objection to the treatment or complaint of its effects is very much less than with cardiazol. The injection with its unremembered sequelæ is not liked by many. The most intelligent patients when recovering give the objection that many normal people have for anæsthesia—they do not like losing consciousness. But the better the result, the more the tendency to admit that conscious improvement follows the treatment. Less promising cases respond with apathy. A very few subjects more paranoid in outlook meet it with protest, which is amenable to reasoning. None in this series showed the wildly excited apprehension which was not infrequent with cardiazol. As a result of this, premedication, apart from the occasional use of atropine, is unnecessary. As other writers have mentioned, the use of drugs of the barbiturate series in the twelve hours before the administration of azoman is contra-indicated because it renders the injection abortive. On one occasion a patient was given medinal gr. 10 during the night. At 8 a.m. the following morning azoman 1·25 c.c., which had previously been a constant convulsant dose, was given intravenously without effect; consecutive supplements of 0·5 c.c. and 0·6 c.c. intravenously were then needed to produce a convulsion. On the next occasion 1·5 c.c. intravenously was followed by two convulsions, and thereafter 1·25 c.c. again became the regular dose. Where sedatives are needed paraldehyde or hyoscine are available and exercise no antagonism.

Non-reactors.

Only one such case has been encountered. A progressive increase up to 4 c.c. intravenously was called for in order to produce a convulsion. Thereafter 4 c.c. intravenously and a supplement of 2 c.c. intramuscularly only produced wild excitement and the case was abandoned.

SUMMARY.

1. Thirty-seven patients have been subjected to convulsion therapy with azoman.

2. Increased delicacy of dosage, absence of sclerosis, small bulk, slow speed of injection, choice of route and reduction of unpleasant subjective sensations make azoman a more satisfactory convulsant than cardiazol.

3. No complications have occurred with azoman which have not been recorded with cardiazol. Control of them is described.

I am indebted to Dr. K. K. Drury, Medical Superintendent of the Leicestershire and Rutland Mental Hospital, for permission to publish this record.

REFERENCES.

WALK, A., and MAYER-GROSS, W.—*Lancet*, 1938, i, p. 1324; *Journ. Ment. Sci.*, 1938, lxxiv, p. 637.

MCGUINNESS, J. P.—*Lancet*, 1939, i, p. 508.

STALKER, H.—*Ibid.*, 1938, ii, p. 1172.