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Correspondence

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TREATMENT OF OBSESSIONAL ILLNESSES AND PHOBIC ANXIETY STATES WITH CLOMIPRAMINE

DEAR SIR,

I hope you will allow me the use of the Correspondence columns to draw the attention of readers to some interesting results we have been obtaining in the treatment of obsessional illnesses, phobic anxiety states and the illnesses which fall in the shaded area between these two.

Our attention was attracted by reports of successful treatment of obsessional states by the administration of clomipramine (Anafranil, Geigy) by slow intravenous drip. Those who had commented on this (Capstick (1), Fernandez Cordoba and Lopez-Ibor (2), Guyotat *et al.* (3), Jimenez (4), Laboucarie (5) and de Voxvrie (6)), had, however, reported relatively few cases; but all had been impressed by the results except Laboucarie, who had given his treatment to only two obsessional cases in his series with one good response only and that when the treatment was combined with E.C.T.

We were encouraged by the majority of these reports to develop a régime for the high intravenous dosage of clomipramine in a variety of clinical conditions with a view to assessing those most likely to respond.

There have often been observed superficial similarities in the thought pattern of patients suffering from obsessional illnesses and those suffering from phobic anxiety states. It has been remarked that these two conditions are but the two ends of a spectrum, and that in between fall phenomena that partake of characteristics from both categories (7). We have therefore been led to extend the treatment to the phobic anxiety states; we have in fact treated more patients suffering from these than from any other disorder. So far 24 patients have been treated, each being given between 6 and 18 intravenous administrations; the dose rises rapidly over the first five days from 50 to 250 mg., given over a period of up to three hours. The clomipramine was given during weekend breaks orally in a daily dose of about 300 mg., the intravenous administrations being resumed on weekdays with a dose rising in some cases to 325 mg. The vehicle used has been 300–500 ml. of normal saline, as the 5 per cent isotonic dextrose which was used initially and which has been recommended by other investigators was found to be locally irritant in some cases.

Six patients responded not at all or only in very slight degree. Two of these were suffering from depression with well-marked hysterical features, one from a manic-depressive psychosis with frequent mood swings, one from a depression with mixed features of an endogenous and reactive illness, one from a personality disorder of psychopathic type, and one from a phobic anxiety state with fairly well-marked hysterical features. The other 18 patients have done very well indeed, 12 of them having experienced complete remission of symptoms and 6 a very considerable degree of relief. Four were presenting with clear-cut obsessional illnesses with compulsive behaviour, and the rest were suffering from phobic anxiety states, some with obsessional symptoms, all of which were severely limiting their lives.

Previous treatment, which had ranged from the use of minor tranquillizers to leucotomy, and had included behaviour therapy in some cases, had either proved ineffective, or had produced only temporary relief.

When a satisfactory result has been obtained, the intravenous administration of clomipramine has been stopped and oral medication continued; in most cases the dose was reduced from 300 mg. daily to 150 mg. daily by 25 mg. amounts every three days. Further slow reductions have been arranged when patients have been seen for follow-up in the outpatient clinics. One patient stopped taking clomipramine altogether, but a recurrence of symptoms after a few weeks decided her to resume a low oral dosage.

The commonest side effects seen have been dry mouth, tremor, constipation and difficulty in accommodation. One patient had two grand mal attacks, but E.E.G. studies were being carried out and she was noted to have had a slightly abnormal E.E.G. before treatment began. This patient and her husband were, however, so impressed by her progress that they both requested that her treatment should not be interrupted because of the epileptic attacks.

Our longest follow-up has now been for six months,

and so far, apart from the patient who stopped all treatment, no relapses have been observed.

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LACTATE-INDUCED ANXIETY: THERAPEUTIC APPLICATION

DEAR SIR,

We read with interest the paper on 'Anxiety and the Effects of Sodium Lactate Assessed Clinically and Physiologically' by Desmond Kelly, Nita Mitchell-Heggs and Daniel Sherman, published in the *Journal* for August 1971 (7). We should like to take the opportunity of answering some of the questions raised by the authors, and also to record that we have developed a new method of treatment.

For the past three years, following the report of Pitts and McClure (9), we have undertaken an ongoing study of intravenous lactate infusion and anxiety. This has so far involved the infusion of 66 subjects with sodium lactate. Thirty-three subjects (24 patients and 9 normal volunteers) took part in a study designed to test the reliability of panic reproduction as described by Pitts and McClure, with physiological, biochemical and endocrinological measurements simultaneously recorded. The effect of medication (propranolol) on psychological state as well as on physiological measurements during lactate infusion has also been assessed (1). Arising from our results a new method of treatment for long-standing intractable, non-situational anxiety was devized and applied to a further series of 33 patients.

Our research method differed somewhat from those reported. We found it impossible to administer the calculated dose of 10 ml./kilogram of $\frac{1}{2}$-molar sodium lactate within 20 minutes while maintaining a constant drip-rate; accordingly we switched to the use of 5 ml./kilogram of 1-molar lactate. As a control procedure with each subject a preliminary experimental session was held in which a volume of normal saline was infused equivalent to that required for the body-weight-related infusion of sodium lactate. The two infusions were separated by exactly one week and given at the same time of day under identical conditions and using the same psychological and physiological measurements. Care was taken to avoid the pre-menstrual week in women. Heart-rate, respiration-rate, electrical skin resistance, skin temperature over both α- and β-adrenergic receptor areas and muscle tremor (by surface electromyography) were monitored continuously. In some of the subjects, reaction-time, plasma lactate, phosphate, bicarbonate, calcium, cortisol and growth hormone were estimated at known intervals.

There were no significant symptoms with the saline infusions. With the infusion of lactate the manifestations of symptoms in our patients were more similar to those observed by Kelly *et al.* than to those reported by Pitts and McClure, and included paraesthesiae, tremor, a sense of vibration, palpitation and dysphoria. The time after beginning lactate infusion at which our patients experienced symptoms (mean 14 minutes) was also closer to Kelly's observation. It would appear that the strict attention paid to a constant drip-rate throughout the 20 minutes (not stressed by Pitts and McClure) may account for this.

Mean scores on the Middlesex Hospital Questionnaire (4) are comparable:

	Free-floating anxiety	Phobic	Obsessional	Somatic	Depressive	Hysteric
Kelly *et al.*	12·4	9·4	10·8	10·4	8·3	6·6
Bonn *et al.*	13·2	10·0	11·3	11·2	7·5	5·7

We also devized a special self-rating scale for anxiety (Normal < 10), and the mean scores were:

Pre-NaCl	30·6	Post-NaCl	30·0
Pre-Lactate	29·1	Post-Lactate	55·2

However, in some important respects our findings differed from those of Kelly and of Pitts and McClure. For example, none of our patients reported an exact reproduction of their 'natural' anxiety attacks in association with lactate infusion. Using Pitts and