Dracard Electrodes.—These electrodes are recommended for routine use. They are simple to apply and worked well initially and over a week. They did not produce severe skin reactions, had the smallest radiological opacity, and cost only 6d. each. After 48 to 72 hours their plaster began to wrinkle, allowing the electrode jelly to dry, so that the trace became unsatisfactory and some electrodes then needed replacing. The number of replacements, however, was not excessive (Table II). Skin reactions due to the edge of the electrode gauze pressing into the skin (Hill and White, 1968) were rare.

Smith and Nephew Electrodes.—SN electrodes are a type of "multipoint electrodes," which have a nutmeg-grater electrode plate whose points penetrate the epidermis, so that electrode jelly is unnecessary (Lewes, 1965b). They were the simplest and quickest electrodes to apply and produced a satisfactory initial trace of adequate duration. A pricking sensation was commented on by some patients. Severe skin reactions appearing in 12 to 48 hours were far commoner with SN electrodes than with any other electrode type (Table III). The reactions were partly due to the electrode plaster, for they were less common when these electrode plates were secured with Dracard plaster. Some reactions were pustular, but swabs of the lesions were sterile on culture. Though reactions have not occurred with their use over a few hours (D. W. Hill, personal communication, 1969), for periods exceeding 12 hours monitoring with SN electrodes is considered unsuitable.

Devices and TEM Electrodes.—These electrodes consist of a metal stud within the dome of a polyethylene cup which contains electrode jelly or a sponge. This design is claimed to reduce movement artifacts (Boter *et al.*, 1966). The small size of metal electrode and its lack of direct contact with the skin, however, are believed to be responsible for a poor initial performance (Table II). Their method of attachment to the skin was relatively complicated, but they rarely became displaced, so that electrode replacements were usually for correction of A.C. interference. The positioning of DE electrodes below the nipple (Fluck and Burgess, 1966) is unsuitable for women, as the edge of the electrode disc tends to cut into the skin of

the breast. Monitoring was relatively expensive with TEM electrodes, and the use of sponge instead of electrode jelly was not found to have any special value.

Cardiac Recorders Electrodes.—The very short duration of action of CR electrodes (Fig. 2) was due to the electrodes becoming displaced. The plaster adhesiveness was poor, and the direct attachment of the lead terminal above the electrode caused the electrode to rise up off the chest with movements of the lead. CR electrodes were easy to apply, gave a satisfactory initial trace, and did not produce severe skin reactions.

Electronics for Medicine and United Aircraft International.—Both these electrodes gave a satisfactory initial trace of average duration. Neither produced severe skin reactions; UA electrodes gave the least skin reactions of all the electrode types. From EM electrodes appears a bare-ended wire to which a connexion has to be attached before monitoring can start, which is inconvenient and time-wasting. EM electrodes tended to slip out from under the adhesive pad attaching them to the skin. Monitoring with UA electrodes was relatively expensive.

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Preliminary Communications

Low Serum Pseudocholinesterase Levels Complicating Treatment with Phenelzine

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Summary: Four patients undergoing treatment with phenelzine developed low serum pseudocholinesterase levels. In one of the patients an apnoea of one hour followed modified electric convulsion therapy. In three cases investigations showed that the serum pseudocholinesterase levels returned to normal after withdrawal of phenelzine.

INTRODUCTION

The monoamine oxidase inhibitors form a valuable method of treating depressive illness, particularly of the neurotic type. Unfortunately, as well as exerting beneficial effects, these drugs are associated with sensitivity reactions—for example, jaundice and other potentially dangerous complications—due to drug interactions such as those which occur with pressor agents

(Dally, 1962), tricyclic antidepressants (Singh, 1960; Nymark and Nielsen, 1963), and analgesics (Shee, 1960; Pells Cocks, and Rossmore-Rowe, 1962; Taylor, 1962).

When phenelzine was introduced in 1959 Bleaden and Czekanska (1960) reported the cases of two patients who, while undergoing treatment with phenelzine, were given electric convulsion therapy (E.C.T.) and developed "alarming" reactions a few minutes after an apparently normal recovery from their seizure. Disordered respiration—in one case breathing stopped, and in the other it became shallow—and a slow and weak pulse were noted. Both patients responded to injections of nikethamide and positive-pressure ventilation with oxygen. Of the two cases one was taking phenelzine at the time of the reaction, while the other had discontinued treatment five days previously after a month on phenelzine 135 mg. daily, a dose substantially above that usually prescribed. As E.C.T. in one patient was modified and in the other was unmodified, the authors assumed that the reaction was not due to phenelzine altering the action of thiopentone or suxamethonium but was the result of the E.C.T. itself.

Goldman (1960), discussing this report, considered the reaction characteristic of "respiratory sluggishness" associated

with the use of muscle relaxants. Commenting on his own experience of over 100 patients who were having treatment with either phenelzine or imipramine combined with E.C.T., Goldman stressed that he avoided the use of muscle relaxants because of their tendency to cause respiratory embarrassment.

Apnoea as a complication following modified E.C.T. is relatively uncommon. Standard textbooks of psychiatric treatment (Sargent and Slater, 1964; Dally, 1967) make no mention of E.C.T. being contraindicated or carrying a greater risk in patients under treatment with the monoamine oxidase inhibitors. If the patient is severely depressed or suicidal they recommend that E.C.T. be given as well as antidepressants, provided the anaesthetist is informed of the nature and dosage of the drug.

Results of Treatment

Drugs	No. of Patients	Serum Pseudocholinesterase Level	
		40+ Units	< 40 Units
Phenelzine	10	6	4
Other monoamine oxidase inhibitors (tranylcypromine, isocarboxazid, mebanazine) .. .	12	12	0

The sigma modification of the Rappaport (Rappaport *et al.*, 1959) method was used to measure pseudocholinesterase levels. Normal limits range between 40 and 80 units.

The finding of low serum pseudocholinesterase levels in patients under treatment with phenelzine prompted an investigation into the enzyme levels of patients in hospital having treatment with one or other of the monoamine oxidase inhibitors. A total of 22 patients were available (see Table), including the four cases reported below.

CASE 1

A woman aged 31 with disabling neurotic symptoms was treated with phenelzine 30 mg. daily for five months, and seemed to respond well. At the end of this time, because of relapse, the dose was increased to 45 mg. daily. One month later, owing to increasing

Pseudocholinesterase levels in Cases 1 to 3.

depression, she was given modified E.C.T. After the seizure the patient remained apnoeic for about one hour, during which time she was ventilated with oxygen. Routine monitoring of pulse and blood pressure showed no abnormality. After an hour she started to breathe spontaneously and there was no further complication. The serum pseudocholinesterase level was found to be 4 Rappaport units (see Chart).

During four courses of modified E.C.T. uncomplicated by phenelzine therapy given in the previous seven years recovery in this patient had always been uneventful. At the time of the apnoea she was on phenelzine 45 mg. daily and trifluoperazine 6 mg. daily and had been taking both drugs continuously for six months. As a result of the apnoea, phenelzine was discontinued. Serum pseudocholinesterase estimations showed that seven days after phenelzine was withdrawn the enzyme level had risen to 18 Rappaport units, and 14 days after its withdrawal the level had risen to 60 Rappaport units. At this stage modified E.C.T. was resumed without prolonged apnoea after the administration of suxethonium. Subsequent pseudocholinesterase levels remained above 40 Rappaport units. Physically the patient has remained in good general health.

A haemoglobin estimation showed a mild hypochromic anaemia—haemoglobin 10.3 g./100 ml. She had not lost weight and gave no history of any complication after anaesthesia. Liver-function tests, including serum bilirubin, alkaline phosphatase, thymol turbidity, thymol flocculation, total protein estimation, serum transaminase (S.G.O.T. and S.G.P.T.), and protein electrophoretogram, were normal apart from the low pseudocholinesterase level, which has been said to be a relatively sensitive indicator of liver dysfunction (Hunt and Lehmann, 1960).

CASE 2

A woman aged 22 was admitted to hospital with a severe puerperal depression. As well as treatment with nortriptyline 75 mg. daily, a tricyclic antidepressant, she was given modified E.C.T. Recovery after treatment was rapid and uncomplicated. Ten weeks later because of a relapse her treatment was changed to phenelzine 45 mg. daily and diazepam 15 mg. daily. Her depression responded to the change of medication, but for social reasons she remained in hospital, and four months after starting treatment with phenelzine a serum pseudocholinesterase estimation showed a plasma level of 12 Rappaport units. Phenelzine was discontinued, and within one month her pseudocholinesterase level had risen to 69 Rappaport units. She was in good health, had not lost weight, was not anaemic, and her liver-function tests were normal.

CASE 3

A 45-year-old diabetic woman on 64 units of insulin zinc suspension daily was admitted to hospital with a neurotic depression. Her depression responded to a course of modified E.C.T., and post-treatment recovery was uncomplicated. Because anxiety and phobic symptoms persisted, she was put on diazepam 15 mg. daily and phenelzine 45 mg. daily. Seven days after starting treatment the pseudocholinesterase level had fallen to 17 Rappaport units. Phenelzine was stopped and another monoamine oxidase inhibitor, tranylcypromine 20 mg. daily, was prescribed. One month later her serum pseudocholinesterase level had risen to 44 Rappaport units. Subsequent levels remained about 40 units. Liver-function tests were normal, and apart from her diabetes mellitus she was in good health.

CASE 4

A woman aged 45 was admitted to hospital with a severe depressive illness. She was treated with amitriptyline 250 mg. daily, and after six weeks this was combined with a course of modified E.C.T. Her recovery from each treatment was rapid. Because of persisting depressive symptoms her treatment was changed to phenelzine 45 mg. daily combined with diazepam 15 mg. per day and a tricyclic antidepressant, trimipramine, 100 mg. at night. After one month the dose of phenelzine was increased to 60 mg. daily. Six weeks later—that is, 10 weeks after starting treatment with phenelzine—her serum pseudocholinesterase level was 25 Rappaport units. One week later she discharged herself from hospital, and it has not been possible to arrange follow-up studies. The patient was not anaemic, had not lost weight, and at the time of her discharge was in good physical health.

MANAGEMENT OF E.C.T. AND ANAESTHESIA

The method used in this unit is to give atropine 1.2 mg. intravenously followed immediately by methohexitone sodium—the four patients in this report receiving 70 to 80 mg. Suxethonium bromide 90–120 mg. is then injected. When the muscular twitching has stopped the patients are ventilated gently with oxygen, the shock is administered, and the patients are ventilated again until spontaneous respirations are resumed.

DISCUSSION

Eastham (1967) reviewed the conditions associated with low serum pseudocholinesterase levels but did not mention anti-depressant drugs. Among states associated with a low serum pseudocholinesterase he included severe liver disease, chronic debilitating disease, severe anaemias, cardiac infarction, poisoning with organophosphorus compounds, and familial cholinesterase abnormalities. Low enzyme levels have recently been reported in patients with eczema (Trotter and Fairburn, 1966). None of the three patients studied suffered any of the above disorders.

It is unlikely that any of these patients were among the small group of people, 1 in 3,000 of the population, with inherited low serum pseudocholinesterase levels, as all four patients had previously recovered uneventfully from modified E.C.T. Also, in the three cases where follow-up study was possible low serum pseudocholinesterase levels returned to normal after withdrawal of phenelzine.

Of the three patients who were followed up, one was a diabetic, another had a mild hypochromic anaemia with a haemoglobin of 10.3 g./100 ml., while the third was six months into the puerperium. All three patients were having other drugs—trifluoperazine in Case 1 and diazepam in Cases 2 and 3—but these drugs were continued after phenelzine was stopped, and the pseudocholinesterase level in each case still returned to normal. Regrettably, no pseudocholinesterase levels were estimated before treatment, but there is no suggestion that the pre-treatment enzyme levels were other than normal.

Further work is planned to extend these observations. It is premature yet to conclude that phenelzine does depress pseudocholinesterase levels. Equally it cannot be said that other monoamine oxidase inhibitors do not have this effect.

CONCLUSIONS

Low serum pseudocholinesterase levels, possibly due to a hepatotoxic effect, have been observed in four patients under treatment with phenelzine. After withdrawal of phenelzine the enzyme level returned to normal in the three cases where investigation was possible. For the great majority of patients on phenelzine and other monoamine oxidase inhibitor anti-depressant drugs, modified E.C.T. is a safe procedure. At the same time, in view of these findings and their implications, when patients who require relaxation with a short-acting muscle relaxant have been on phenelzine either in high dosage or for prolonged periods it would seem a reasonable precaution to estimate first the serum pseudocholinesterase, so that if necessary anaesthetic techniques may be modified to avoid untoward complications.

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Medical Memoranda

Virus Antibody Levels in Multiple Sclerosis

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In a previous study (Ross *et al.*, 1965a) single sera from 96 cases of multiple sclerosis and from 96 matched controls were examined for complement-fixing antibodies to herpes, mumps, psittacosis-lymphogranuloma venereum group, Q fever, measles, varicella-zoster, poliovirus type 1 and type 2, and *Mycoplasma pneumoniae*. Complement-fixing antibody for each of the agents was consistently present in a greater number of patients than controls, though a statistically significant difference was obtained only with varicella-zoster. Several possible explanations were suggested for these findings—namely, that patients with multiple sclerosis might show a difference in immunological response to infective agents, that patients with

multiple sclerosis might be particularly susceptible to infection with varicella-zoster, and that infection with varicella-zoster or an antigenically related virus such as herpes simplex (Ross *et al.*, 1965b) might be associated with the aetiology of multiple sclerosis. Other workers have shown significantly higher measles antibody titres in single sera from multiple sclerosis patients than from controls (Sibley and Foley, 1965; Pette and Kuwert, 1965; Adams, 1967) and have suggested that infection with measles virus may have an aetiological relationship with the disease.

PRESENT STUDY

Following these studies on single sera it seemed relevant to investigate antibody levels in serial sera from patients with multiple sclerosis, since it seemed that if a virus such as measles, varicella-zoster, or herpes simplex were directly associated with the aetiology of multiple sclerosis that virus might remain latent in the central nervous system and its reactivation might be