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Correspondence

Correspondents should note that space is limited and shorter letters have a greater chance of publication. The Editors reserve the right to cut letters and also to eliminate multitudinous references. Please try to be concise, strictly relevant and interesting to the reader, and check the accuracy of all **references in Journal style.**

TREATMENT OF NEUROLEPTIC MALIGNANT SYNDROME

DEAR SIR,

Dr Scott (*Journal,* January 1984, **143,** 98) drew attention to treatment of the neuroleptic malignant syndrome (NMS) with dantrolene sodium, a peripheral muscle relaxant. There is another and perhaps more pharmacologically logical treatment available. Indirect evidence is available that NMS is caused by a relative postsynaptic receptor dopamine depletion (White, 1983). Bromocriptine, a postsynaptic dopamine agonist, has been used successfully as a treatment in NMS (Mueller *et al,* 1983).

There have been two other recent reports of the use of bromocriptine. Zubenko and Pope (1983) successfully used 30 mg per day on a patient who had been on depot fluphenazine decanoate and lithium. A significant response was noted within six hours, blood pressure and temperature were normal within three days. A relapse occurred within five days of reducing the dose to 5 mg per day. An increase of dose resulted in "a rapid remission".

Interestingly, Granato *et al* (1983) used both dantrolene sodium and bromocriptine. The patient had been receiving fluphenazine decanoate and benztropine. They found that intravenous dantrolene sodium (0.8 mg per kilogram body weight) every six hours abolished the fever and made the creatine phosphokinase level normal. However, rigidity, tremulousness and obtundation remained. Amantadine in a dose of 300 mg per day had no effect, but bromocriptine, at a maximal dose of 60 mg per day, was associated with a marked improvement in muscle tone and tremor, within two days.

It therefore seems likely that both bromocriptine and dantrolene sodium may have a place in the specific treatment of the NMS. The problem of future relapse of psychosis remains. If the use of neuroleptics is unavoidable, first attempts could include use of a less potent dopamine antagonist and avoidance of depot preparations. Use of the original neuroleptic introduced gradually in small doses is more controversial. Use of oral dantrolene sodium as prophylaxis with a neuroleptic has not been reported and could be contemplated. Bromocriptine as prophylaxis may be similarly considered, if one accepts the doubt that the antipsychotic effect of neuroleptics is mediated via central dopamine receptor blockade (Marsden and Jenner, 1980) although the present evidence is to the contrary (Crow, 1980).

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TREMOR OF THE EYELIDS

DEAR SIR,

I was interested to read the letter from Dr Freed in your correspondence column, on rapid tremor of the eyelids after overdose of fluphenazine (*Journal,* November 1983, **143,** 525–26).

I have recently seen a patient who developed rapid tremor of the eyelids after therapeutic doses of haloperidol, given for an acute relapse of a schizophrenic illness. The patient is a 43-year-old woman with an 11 year history of schizhophrenia, treated with a variety of drugs including chlorpromazine, trifluoperazine, fluphenazine and flupenthixol. She had often experienced tremor in her limbs as a side effect of this medication, but had never had any ocular side effects.

She was readmitted in December 1983 with a relapse of her schizophrenic symptoms and commenced on haloperidol 5 mg b.d. and procyclidine 5 mg b.d. Eighteen days after haloperidol was commenced, the patient complained of "flickering lights" and was noticed to have severe rapid twitching of both eyelids accompanied by a tremor of both arms and legs. Oral procyclidine did not seem to improve the eyelid tremor to any appreciable extent, but it stopped spontaneously a week later when haloperidol was changed to Thioridazine 100 mg od.

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THE DST—A DIAGNOSTIC MIRAGE?

DEAR SIR,

The dexamethasone suppression test (DST) has been under investigation for nearly 15 years, yet neither its reliability nor its validity are clear.

Reputable and scientifically rigorous workers in many centres have tested the claims of Carroll *et al* (1981). Notwithstanding the allowances which have to be made for varying diagnostic concepts, there is still a marked and disturbing lack of consistency in the research findings. These reflect on both the test specificity and sensitivity. For example high rates of non-suppression have been reported for mania, neurotic depression, alcoholism, dementia, anorexia nervosa and even in 'healthy' control subjects. These generally widely diverse and discrepant findings must raise the haunting spectre of psychiatry once more embarking upon the false pursuit of a Holy Grail.

We therefore set out to document the range of serum cortisol values associated with depression and other selected, DSM III based diagnostic groups and to assess the response of serum cortisol to the administration of a standard DST.

One hundred adult patients receiving diagnoses (per DSM III criteria) of major depression (38), dysthymia (19), mania (13), schizophreniform disorder or schizophrenia (30) were accepted into the study provided that they had none of the contraindications to a valid DST.

A 4.00 p.m. baseline serum cortisol (Diagnostic Products Corporation, RIA) determination was performed a minimum of 48 hours after admission. That evening 1 mg of dexamethasone was given at 11.00 p.m. and blood samples for cortisol analyses were taken the next day at 1600 and 2300 hours.

Results: The mean base-line blood cortisol levels did not differ significantly between the groups major depression, dysthymia, mania and schizophrenia. Most groups have followed Carroll's lead and adopted the 138 nmol/l (5 μg/dl) criteria for non-suppression. At that level our rates of non-suppression were, major depression 38 per cent, schizophrenia 20 per cent, mania 46 per cent and dysthymia 32 per cent. However, inspection of our data for major depression indicated that a cut off at 210 nmol/l gave the best compromise between specificity (83 per cent) and sensitivity (38 per cent). The rates of non-suppression were then markedly lower in the non-depressed (schizophrenia 10 per cent, mania 31 per cent, dysthmia 16 per cent).

The fact that the rate of non-suppression for major depressive illness was very much lower than the rate found by Carroll *et al* (1981) could reflect the broader group subsumed under that DSM III label. The relatively high rates of non-suppression in the other diagnostic groups, consistent with the work of many others, needs explaining.

For test specificity the base population definition is important. Specificity in this case is the rate of suppressors in persons who do not have the disorder. Is that latter category (the non-disordered) to be the general, normal population, which is not very relevant in the clinical situation; or is it the non-depressed psychiatric patient population; or is it the non-melancholic, but depressed population?

Our results, and those of a number of other workers, do not support the use of the test as a (specific) pointer towards the diagnostic label of depression, in a general psychiatric population. There are positives in too many patients appropriately classified elsewhere. The high rate of non-suppression in other disorders also militates against placing any reliance on this test in those particular clinical situations where our current phenomonologically based diagnostic criteria are most vulnerable. For example the high rate of non-suppression in the demented renders the test useless in distinguishing the pseudo-demented. It would appear that the dysthymic can not be clearly separated from those with major depression.

The evidence concerning the value of the dexamethasone suppression test is consistent with the idea that non-suppression may simply be a measure of the severity of the clinical state. Relative non-suppression of cortisol could reflect the degree of that person's