suffered a serious side effect compared to over 90% of phenelzine treated patients. Thirty eight per cent of patients had two or more serious side effects and all except one were taking phenelzine. Altogether 132 major side effects were recorded for 141 patients treated with phenelzine.

The risks of MAO inhibitors will be further increased in an era of 'prophylaxis' and long-term treatment. Recent studies have shown that withdrawal effects are more serious than with tricyclics (Tyrer, 1984) and overdose is extremely difficult to manage (Linden et al, 1984).

The most remarkable feature of the above study was that in a second article (Rabkin et al, 1984) the authors were able to conclude that 'MAO inhibitors when properly prescribed are safer than is often believed'. This chemophilic conclusion seems to be supported by Dr. Pare's treatment of the risk to benefit ratio for these drugs. For the sake of the patients to whom we prescribe I hope that a more careful view will prevail so that we learn from the lessons of history without repeating them. This is the second time around for the MAO inhibitors but the millenium has not arrived.

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# Cyproheptadine and Antidepressant-induced Anorgasmia

SIR.

Anorgasmia in women is a recognised side-effect of clomipramine (Anafranil data sheet) and has been

reported with imipramine (Sovner, 1983). We report two cases of anorgasmia, one induced by clomipramine, the second by imipramine, which resolved with cyproheptadine. A third patient who had imipramine-induced anorgasmia failed to respond to this treatment.

Case 1: Mrs E. T., aged 36 years was prescribed clomipramine for depression. The dose was started at 25 mg nocte and increased to 75 mg. Within two weeks of starting this treatment she experienced anorgasmia. She could become sexually aroused but was unable to achieve orgasm either during intercourse or by masturbation. This situation had persisted for three months during which time clomipramine 75 mg nocte was continued. A reduction to 50 mg nocte did not improve her sexual functioning. She continued to take clomipramine 50 mg nocte and was given a supply of cyproheptadine 4 mg tablets with instructions to take one tablet ninety minutes before anticipated sexual activity. If after trying this on four occasions she was still anorgasmic she was to progressively increase the dose. The first time that she took 8 mg cyproheptadine she experienced orgasm in response to masturbation. So long as she takes cyproheptadine 8 mg before sexual activity she is orgasmic. She failed to achieve orgasm after taking placebo tablets which she was told were cyproheptadine

Case 2: Miss A. C., aged 22 became depressed after a broken love affair. She was treated with imipramine, starting with 25 mg nocte and increasing to a total daily dose of 100 mg. Within a week of increasing the dose to 75 mg she experienced anorgasmia during masturbation, her only form of sexual outlet. She had previously been multiorgasmic and had regularly masturbated 3-4 times a week. She continued to take imipramine 100 mg daily and was given a supply of placebo tablets. She was told to take these tablets ninety minutes before masturbation, increasing the dose from one to four tablets. This did not resolve the anorgasmia. She was then started on cyproheptadine and became orgasmic when she took 12 mg before masturbation (the placebo tablets did not match the active tablets).

Case 3: Mrs W. M., aged 28 had been taking imipramine 150 mg daily for depression for six months. During this time she consistently failed to achieve orgasm. Before starting this treatment she was coitally orgasmic on about 50% of occasions. She was given placebo tablets and then cyproheptadine tablets as in Case 2. Neither the placebo nor cyproheptadine 8 mg resolved the anorgasmia. Drowsiness induced by the cyproheptadine prevented further increments in dose. Desipramine 100 mg daily was substituted for the imipramine but this change of treatment did not resolve the anorgasmia. She was then weaned off anti-depressants and again became orgasmic.

The physiology and pharmacology of sexual function are poorly understood. Animal studies have implicated a 5-hydroxytryptamine (5HT) as one of the likely neurotransmitters involved in the control of sexual responses, and this amine probably has an inhibitory role. Clomipramine and imipramine inhibit the re-uptake of 5HT, but also exhibit anticholinergic and alpha adrenoceptor antagonist activity. Cyproheptadine is a 5HT receptor antagonist. In two of the three cases reported cyproheptadine reversed the inhibiting effect of the anti-depressant on orgasm. These observations suggest that anti-depressant-induced anorgasmia results from the effect of these drugs on 5HT activity. Sovner (1984) also reported a case of tricyclic anti-depressant-induced anorgasmia which was reversed by cyproheptadine. More recently, Decastro (1985) successfully reversed MAOIinduced anorgasmia in a male with cyproheptadine.

In Case 3 the patient was prevented from increasing the dose of cyproheptadine by the occurrence of side-effects. Treatment with imipramine was changed to desipramine because Sovner (1983) reported the case of a woman who experienced anorgasmia with imipramine but not with desipramine, but in our case this change of treatment was ineffective in restoring orgasmic attainment.

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# Depression and Urinary Free Cortisol DEAR SIR.

The article by Dr R. J. Dolan and colleagues, "Life events, depression and hypothalamic-pituitary-adrenal axis function" (*Journal*, October 1985, 147, 429–433) reports some differences in urinary free-cortisol excretion between patients with and without severe life events or with and without marked difficulties.

It seems important to point out, however, that the actual 24 hour urinary free cortisol (UFC) excretion values (µg/24 hours) were unusually high in all these patients, whether or not adverse life events and difficulties were present. All the mean values are

greater than 145 µg/24 hours. In most other studies the mean UFC excretion of normal subjects is about 40 to 50 µg/24 hours and in depressed patients the values rarely exceed 100 µg/24 hours (Carroll et al, 1976). The values given by Dr Dolan and associates are all well within the range expected for patients with Cushing's disease.

The authors stated that they used a radioimmunoassay procedure for their UFC analyses. The results call into question the validity and specificity of their assay or of the laboratory procedure they adopted. These considerations also would tend to raise questions about the validity of their plasma cortisol assays for assessing DST status of the subjects (Ritchie et al, 1985).

Radioimmunoassays for cortisol vary widely in their performance. For this reason, validation of the assay by establishing local norms always is to be encouraged.

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## Complaints of Inability to Sneeze

DEAR SIR,

Shukla (Journal, November 1985, 147, 564-565) suggests asneezia as a previously unrecognised psychiatric symptom, yet fails to distinguish between the patient with a genuine absence or reduction in frequency of sneezing and the patient who complains of such but in whom there is no objective change. In the absence of this distinction, an alternative explanation is that he is reporting culturally determined hypochondriacal overvalued or delusional ideas. The following observations support this view.

Firstly, Dr Shukla highlights the importance of sneezing within Indian culture and it is well known that the content of such ideas is culturally dependent (Hamilton, 1974). Secondly, there were significant differences between the educational and socioeconomic backgrounds of the asneezic and the control groups, and it has been widely suggested that patients of lower socio-economic groups and educational achievement are more likely to present with