DANGERS OF REDUCING LITHIUM

DEAR SIR,

We were interested but not surprised at the article and letter regarding the dangers of manic relapse following lithium withdrawal (*Journal*, October 1982, **141**, 407–10, and 431). The existing literature regarding this known hazard made us concerned about the nature of the investigation undertaken by Drs Margo and McMahon and we looked in vain for an indication in their article that the patients involved in their study had given their informed consent.

More attention has been paid to the advisability of maintaining patients on long-term lithium treatment, particularly following the recent concern about the effect of lithium on renal structure and function. Three years ago we started a prospective investigation to determine whether patients maintained on lithium would remain well if their lithium levels were maintained below the (then) recommended minimum serum lithium level of 0.6 mmol/l. In an initial pilot study we reduced the lithium dosage in 29 patients suffering from affective disorder who had been maintained on lithium for a period of 1 to 12 years (mean = 6.7 years). Twenty-five patients suffered from bipolar affective illness, four were unipolar. These patients were part of 165 patients who regularly attended the New York University/Bellevue Center Affective Disorders Clinic and were selected on the basis of the patient's wish to reduce his lithium dosage (12 cases); the remaining 17 subjects had impaired renal concentration ability. All patients had remained free of affective episodes since starting lithium apart from one patient who had stopped lithium suddenly in the past and had become manic.

The dose of lithium was reduced so as to maintain a serum lithium level of between 0.3 and 0.7 mmol/l. The patients were seen at 2 weekly intervals for 2 months and then at monthly intervals if there was no sign of mood disturbance. Serum lithium levels were taken at each visit. All patients were taking lithium alone with no other psychotropic drug.

For direct comparison, all other patients in the clinic receiving lithium alone and who had been maintained on the drug without relapse for at least one year were studied as the control group. Forty eight patients fulfilled these criteria. These patients did not differ in the period of time during which they were receiving lithium, maintained serum lithium level, diagnosis, age or sex ratio, from the patients in whom the lithium dose was reduced. These patients continued to attend the lithium clinic at their customary frequency, which ranged from three-weekly to three-monthly intervals.

All patients were monitored for a period of six months. Patients who had an affective relapse, sufficient to warrant additional medication or change of drug, and who scored 60 or less on the Global Assessment Scale were recorded as relapsed cases and treated appropriately.

Of the 29 patients in whom the dose of lithium was reduced 13 relapsed during the 6 month period of study. The mean time of relapse was 12.2 ± 7.4 weeks after lithium dosage was reduced (range 3-25 weeks). All the 11 bipolar patients who relapsed became manic whereas the 2 unipolar patients again became depressed. Two manic patients required admission to hospital. Six of the 48 patients in whom the lithium level was maintained relapsed, 4 of whom became depressed, including 2 bipolar subjects. These results indicate that dosage reduction was a significant factor in causing relapse ($P < 0.01$ χ^2 test with Yates' correction).

Attempts were made to determine whether it was the percentage reduction of dosage which contributed most to relapse, or reduction of lithium dosage below a critical lithium level. There was no significant relationship between either of these measures and likelihood of relapse but 2 patients relapsed even though their new maintained lithium level was as high as 0.7 mmol/l.

The results indicate that it may be hazardous to reduce the dose of lithium precipitously in bipolar patients maintained on lithium for long periods. Lower maintenance serum lithium levels may well be effective in maintaining prophylaxis (Hullin, 1980) but the incremental reduction in dosage should be kept as small as possible to minimize the chance of manic relapse.

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COMMUNITY SCREENING FOR MENTAL ILLNESS

DEAR SIR,

The General Health Questionnaire is widely used for psychiatric screening and for comparing levels of distress in epidemiological research. The claim of Benjamin, Decalmer and Haran (*Journal*, February

1982, **140,** 174–80) that the GHQ is "unsuitable as a screening instrument for mental illness in the community" therefore deserves close scrutiny.

The major criticisms of the conclusion of Benjamin *et al* come under two headings. First, their study was of a small biased sample, and second, they only examined the validity of the 60 item GHQ.

The first feature, that of the biased sample, is an important one because it restricts the appropriateness of generalizing the findings of Benjamin *et al.* There is agreement on the need to revalidate the GHQ when used in different settings or in populations with different characteristics. So at best their conclusion has to be confined to GHQ use on women aged 40–49 who are still able to pass through a 'natural' menopause. To make any more general statement on the validity of the GHQ is bad science. Such general conclusions can only be reached from a consideration of many validation studies of the GHQ, most of which support its continuing use. Specifically, with non-consulting samples the GHQ provides a high validity research tool.

Some versions of the GHQ are demonstrably better and this differential validity is overlooked by Benjamin *et al*, who only consider the GHQ-60. And why "invent" a new 15 item version without assessing the merits of already validated shorter versions with their chosen sample, namely the GHQ-30, GHQ-20, GHQ-12 and GHQ-28? A recently completed study (Banks, 1983) has shown how the validity of the GHQ-30, GHQ-28 and GHQ-12 vary considerably within the same sample. In particular, attention should be drawn to the 28 item GHQ which had a sensitivity of 100 per cent, a specificity of 84.5 and overall misclassification rate of 15 per cent using a cutting score of 5/6.

It is important that clinicians and research workers receive a fair account of the GHQ, and that they understand it is composed of a family of instruments with much better psychometric, screening and validation properties than Benjamin *et al* would have us believe.

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ARE AUTISM AND ANOREXIA NERVOSA RELATED?

DEAR SIR,

I have recently come across 3 cases of males with infantile autism who had female first-cousins with anorexia nervosa. In 2 of these cases the cousins were on the maternal side of the family. I would like to draw readers' attention to this observation and ask if any have noticed a correlation between the rare syndromes of autism and anorexia nervosa.

Two further points are worth mentioning in this context. First, there is now some evidence for a 'biochemical subgroup' of autism showing a particular chromatographic profile with regard to urinary excretion of substances giving absorbancy at 280 nm (Gillberg *et al,* 1982). This chromatographic pattern is now referred to as 'pattern A'. 'Pattern A' is not seen in normal children, but sometimes in childhood psychosis cases other than infantile autism. Also, it has been found in cases with anorexia nervosa (Trygstad *et al,* 1980). This latter point is of particular interest with regard to a hypothesis linking autism and anorexia nervosa. Second, the obsessive insistence on sameness seen in autistic children, is sometimes a striking phenomenon in anorexia nervosa too. Also, anorectic patients quite often show aloofness and problems of social relationships. Is there a possibility that a common biochemical disturbance may interact with other factors (brain damage, starvation, cultural factors) to cause autism in young boys and anorexia nervosa in prepubertal girls?

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FAMILY HISTORY STUDY OF ANOREXIA NERVOSA AND BULIMIA

DEAR SIR,

We regret to report that a number of numerical errors appeared in Table II in our recent article "Family History Study of Anorexia Nervosa and Bulimia" (*Journal,* February 1983, **142,** 133–8). The corrected table is published below.

In addition, the last paragraph of the methods