gain insight into their lives, situations and conditions. This, I would argue, involves allocating responsibility for the condition to the patient and may not resemble the treatments of physical medicine. The reader will note that this conclusion is congruent with that of other students of alcoholism, such as Orford and Edwards (quoted on page 452 of my article), whose "primary clinical experience and responsibility prior to plunging into clinical research" can certainly not be doubted. However, given that such corroborative evidence has emanated from "those commanding the heights (of) Denmark Hill" I fear that Dr Macdonald will remain unconvinced.

PHIL DAVIES

MRC Medical Sociology Unit,
Institute of Medical Sociology,
Westburn Road, Aberdeen

VALIDITY AND USES OF THE GHQ

DEAR SIR,

In your May issue, Tarnopolsky *et al* report (*Journal*, May 1979, **134,** 508–15) on the validity of the GHQ in a community sample. They find lower validity than has been reported in samples of general practitioner patients. This finding might be the result of a feature of their research design. The type of illness measured by the GHQ is often quite fleeting. Thus it has been reported that the correlation between GHQ score and total score on the Present State Examination is .8 when the PSE is conducted within a week of the GHQ, but drops below .5 for a longer interval (Duncan-Jones and Henderson, 1978, p. 235). It is clear there was an interval between the GHQ and the validatory psychiatric interview in Tarnopolsky's study, but the length of that interval is not indicated. Since a matching design was used, the interval cannot have been trivial. There was no such interval in the general practitioner studies. Therefore this difference in design might account for the lower validity.

In presenting their data on screening, Tarnopolsky *et al* make the important point that their data for approximately equal numbers of high scorers and matched low scorers give biased estimates of 'sensitivity' and 'specificity' for the community population, and correct for this by weighting up the low scorers. This would be valid and appropriate if their low scorers were a representative sub-sample of all the low scorers in their original sample. But since they were elaborately matched to the high scorer group, this cannot be so.

It seems possible that the use of matching has weakened this study in two ways. It is feasible to pre-allocate respondents to different sub-sampling classes (prior to first interview) so that (a) subjects for the second phase interview are selected randomly but with probability of selection being dependent on GHQ score, and (b) the first-phase interviewer can determine whether or not a second-phase interview is required, and make a tentative appointment for it. Using this procedure, one can keep the interval between interviews short, and make valid estimates for the whole population from the second phase interview. Details are given in Henderson *et al* (in press).

PAUL DUNCAN-JONES

Social Psychiatry Research Unit,
The Australian National University,
Canberra, ACT 2600

References

DUNCAN-JONES, P. & HENDERSON, S. (1978) The use of a two-phase design in a prevalence survey. *Social Psychiatry*, **13,** 231–7.

HENDERSON, S., DUNCAN-JONES, P., BYRNE, D. G., SCOTT, R. & ADCOCK, S. (in press) Psychiatric disorder in Canberra; a standardized study of prevalence. *Acta Psychiatrica Scandinavica.*

TARDIVE DYSKINESIA AND DEPOT FLUPHENAZINE

DEAR SIR,

I read with interest Dr Nasrallah's letter (*Journal*, May 1979, **134,** 550) in which he suggested that tardive dyskinesia in patients maintained on depot fluphenazine could be caused by irregular release of fluphenazine from the intramuscular depot. In an earlier study (Nasrallah *et al*, 1978) he and his colleagues had found wide fluctuations in plasma fluphenazine concentrations in 10 patients during 2 weeks following a 50 mg injection of fluphenazine decanoate: varying numbers of fluphenazine peaks occurred at random, separated by periods in which little or no drug could be detected. (Their analytical procedure, gas-liquid chromatography, could measure fluphenazine concentrations above 3 ng/ml). Dr Nasrallah went on to propose that during depot fluphenazine treatment the decline in plasma fluphenazine levels which followed intermittent peaks could act like a drug withdrawal to cause dyskinesia by producing dopaminergic receptor hypersensitivity.

We have also examined plasma fluphenazine levels in patients receiving fluphenazine decanoate (Wiles and Gelder, 1979). We used a different analytical technique, a radioimmunoassay, which can measure down to 0.05 ng/ml (Wiles and Franklin, 1978). In our study, 33 subjects were receiving chronic treatment with a wide range of doses (12.5 to 150 mg) given at intervals of 1–5 weeks. Our results differ

from those of Nasrallah *et al* (1978) in that we found a regular pattern of plasma fluphenazine concentrations during the interval between injections (Fig 1). Each

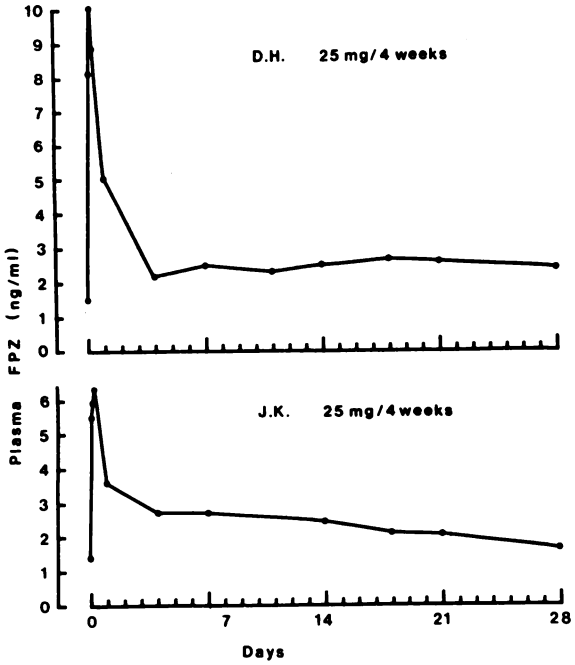

FIG 1.—Plasma fluphenazine 'profiles' after an injection of fluphenazine decanoate in 2 subjects maintained on a regime of 25 mg every 4 weeks. (I would like to acknowledge the help of Drs T. R. E. Barnes and T. Kidger in the study of these patients).

injection was followed by a rapid rise in plasma fluphenazine concentrations to a maximum at 1–8 hours. The height of this peak varied from 1.2 to 12 times the pre-injection level. Within the next 12–36 hours, the plasma fluphenazine fell to a level slightly above that found before injection and then remained stable until the next injection, suggesting a steady release of fluphenazine from the depot over this period. Unlike Dr Nasrallah, we found no wide fluctuations in the plasma fluphenazine level beyond 24 hours post-injection, so that when immediately post-injection levels were excluded the average coefficient of variation for an interval between injections was $\pm$ 18 per cent. Plasma fluphenazine levels during this period were always measurable and average levels which ranged from 0.7 to 16.8 ng/ml were dose-related ($r = 0.84$, $P < 0.001$). Prolactin was also measured in these samples (unpublished data). During the period of stable fluphenazine levels, plasma prolactin was generally elevated beyond the upper limit of the normal range for untreated subjects. Immediately post-injection a further transient increase was found in some cases. Our prolactin results are essentially similar to those of Nasrallah *et al* (1978) who, incidentally, found elevated prolactin levels in samples in which he was unable to detect fluphenazine.

Our findings indicate that during established treatment with fluphenazine decanoate, plasma concentrations of the drug are stable for the majority of the period between injections and in most cases are sufficient to cause measurable dopaminergic blockade. Fluctuations in plasma fluphenazine levels wide enough to produce alterations in dopaminergic blockade occur only within 24 hours of an injection. Therefore, their frequency is determined by the length of the interval between injections. We are currently investigating the possible clinical significance of these fluctuations.

DAVID WILES

Department of Psychiatry,
University of Oxford,
Littlemore Hospital Research Unit,
Littlemore Hospital,
Oxford OX4 4XN

References

NASRALLAH, H. A., RIVERA-CALIMLIM, L., ROGOL, A., GILLEN, J. C. & WYATT, R. J. (1978) Fluphenazine decanoate: plasma concentrations and clinical response. *Psychopharmacology Bulletin*, **14**, 46–7.

WILES, D. H. & FRANKLIN, M. (1978) Radioimmunoassay for fluphenazine in human plasma. *British Journal of Clinical Pharmacology*, **5**, 265–8.

—— & GELDER, M. G. (1979) Plasma fluphenazine levels by radioimmunoassay in schizophrenic patients treated with depot injections of fluphenazine decanoate. *British Journal of Clinical Pharmacology* (accepted for publication).

CONVERSATIONS WITH SCHIZOPHRENICS

DEAR SIR,

Abrahamson and Brenner observe in their patients and in your columns (*Journal*, June 1979, **134**, 648–9) that deterioration occurs early in the course of a chronic schizophrenic illness which they say remains stable thereafter without further progressive deterioration. They therefore wish to correct the traditional view of progressive deterioration throughout the long course of the illness, a view which they claim to detect in my paper (*Journal*, February 1979, **134**, 187–94).

Without adequate longitudinal observation I remain uncertain. The longest I can claim to have known any chronic schizophrenic patients is only seventeen years and they number only six. It is true that I have seen no evidence of further deterioration