with promising clinical improvement). We are currently engaged in a study to pursue this issue in a more scientific manner, and welcome the views of other clinicians.

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Genetic polymorphism and drug-induced movement disorders

Sir: We were interested to read the paper by Armstrong *et al* (1997) on drug-induced movement disorders in relation to the *CYP2D6* genotype. We would agree that this important polymorphism may well be a contributory factor in more chronic drug-induced movement disorders.

Several lines of evidence support this. Firstly, one of the most robust findings in the whole field of tardive dyskinesia (TD) research is the link between TD and high neuroleptic dosage. Impaired clearance of antipsychotics due to the poor metaboliser genotype leads to elevated plasma levels, which has clear implications in view of the first association. Other studies have attempted to assess the problem from a different standpoint: looking at the variation in neuroleptic breakdown between those with TD and schizophrenic controls. The best study in this area is that of Yesavage *et al* (1987), which found a significant difference in standardised thioxanthine levels between 21 TD sufferers and 20 controls.

In our recent study (Bates, 1997) we used promethazine, a phenothiazine predominantly metabolised by the CYP2D6 cytochrome, to probe metabolic clearance in 18 patients, 10 with TD and eight controls. We used a high-performance liquid chromatography technique which simultaneously assayed promethazine and its two major breakdown products, the sulphoxide and monodesmethyl metabolites. We found evidence of significant impairment of metabolism of promethazine in the TD group, with raised promethazine levels and raised promethazine to metabolite ratios, indicating this was not an effect of varying absorption or bioavailability. We will be publishing our results more fully soon.

This simple and relatively inexpensive method may prove useful in pretreatment testing to enable prediction of those likely to develop TD or concentration-dependent side-effects, and to guide dosage decisions.

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Demography and age at onset of schizophrenia

Sir: Jablensky & Cole (1997) conclude from their analysis of the WHO 10-Country study of schizophrenia that marital status has a major effect on age at onset of schizophrenia, and that the effect of gender disappears when controlling for marital status (and other variables). However, these findings are partly due to demographic effects. To explain this artefact assume that outbreak of schizophenia occurs (like a random event) irrespective of marital status. As is well known, married people are in our population on average older than single ones. Therefore the mean age at onset of schizophrenia will be later for married people than for single ones. This difference does not reflect a real association between schizophrenia and marriage (which was excluded by the hypothetical model) but it reflects a trival demographic effect due to the different age structures of married and single people. This applies to men and women but in a different way. In general, women marry earlier than men. Thus, in the population, married women are on average younger than married men, and unmarried women are younger than unmarried men. Let us assume that outbreak of schizophrenia is related neither to gender nor to marital status. Then because of these different age structures the mean age at onset will be earlier for married women than for married men. The same relation holds for singles. But, as above, these differences are due to a trival demographic effect. If there is a real association between gender and schizophrenia in the sense that onset is later for women, then this difference is reduced when comparing married women with married men and single women with single men. Thus differences in the age structures between married and single persons in the population explain, at least in part, the effects of marital status and gender on age at onset, described by Jablensky & Cole. The differences in age at onset between developing and developed countries may be attributed to different demographic structures in these countries. We do not deny these effects, but to disentangle demographic effects from real effects the age structures of the underlying population must be taken into account when analysing the data.

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Author's reply: Jennen-Steinmetz *et al* suggest that "differences in the age structures between married and single persons . . . explain, at least in part, the effects of marital status and gender on age at onset, described by Jablensky & Cole". Since the statistical analyses we use uncorrelate gender and marital status prior to examining the relationship of either variable to age at onset, Steinmetz *et al*, can rest assured that no part of our conclusions reflects a spurious correlation between marital status and age at onset of schizophrenia that is induced by those two variables' common association with gender differences in age at marriage. In the general linear model, the effects of gender (and gender-correlated differences in age at marriage) are partialled out, or controlled for, in the calculus underlying multiple regression (Mosteller & Tukey,

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1977). Thus, in our analysis, (a) any variance in marital status that is correlated with gender (and, by proxy, any gender-related differences in age at marriage) is removed, to produce a 'gender-adjusted marital status'; (b) any variance in age at onset that is correlated with gender (and, by proxy, with gender differences in age at marriage) is removed, to produce a 'gender-adjusted age at onset'; and (c) the adjusted relationship between marital status and age at onset is estimated by the correlation between the gender-adjusted marital status and gender-adjusted age at onset described above. As a result, no portion of the association between age at onset and marital status in the models from which we draw our conclusions reflects those two variables' common association with gender differences in age at marriage.

While Jennen-Steinmetz *et al* are correct in arguing that age differentials would induce a simple correlation between marital status and age at onset when gender differences in age at onset and age at marriage exist, our analyses adjust for this effect and continue to identify a significant relationship between marital status and age at onset in schizophrenia.

Mosteller, F. & Tukey, J. W. (1977) *Data Analysis and Regression*. Reading, MA: Addison-Wesley.

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Working on the interface between primary and secondary care

Sir: Gask *et al* (1997) reviewed models of working at the interface between primary and secondary care and concluded that the consultation–liaison model had several theoretical advantages. They commented that factors affecting referral remain poorly understood.

We examined the reasons why eight general practitioners (GPs) based in a deprived area of Liverpool referred patients to a shifted out-patient clinic over a 10-month period. The GPs were contacted as soon as possible after receipt of a referral letter and a semi-structured questionnaire was completed, either by telephone or face-to-face. Data were available on 44 out of 47 of the referrals.

Three-quarters of referrals were initiated by the GP (33 out of 44), while the remainder were made at the request of the patient, their family or other professionals. Around half of the referrals (23 out of 44) were due to a failure to respond to the GP's treatment. Severe mental illness was given as the main reason for referral in only eight cases. The GPs wanted the psychiatric services to take over the management of two-thirds (30 out of 44) of the patients and not to refer them straight back. The GPs usually did this by requesting treatment for their patients but sometimes made it clear that they felt burdened by the patient. Expectations in the 13 cases that the GPs wished to keep on managing were more concrete and included advice on diagnosis, changing the antidepressant and the patient's fitness to work.

The GPs thought that referral was helpful to 73% (22 out of 30) of the patients, 23% (seven out of 30) of the patients' families and 93% (28 out of 30) of the GP practices. GPs rated their overall satisfaction with the referral as 'mostly satisfied' or 'excellent' for 68% (26 out of 38) and 'mixed' in 32% (12 out of 38). The GPs were not asked directly about their reason for satisfaction but in several cases they spontaneously attributed satisfaction to not seeing the patient again.

Our study suggests that an important role of referral may be to reduce the stress or burden on GPs by passing on the responsibility to the psychiatric services. GPs are often more concerned with the minor disorders they see frequently than with the more severe disorders that current policy is directing psychiatrists towards (Department of Health, 1994). There is little evidence that the widespread development of consultation–liaison links with GPs will lead to a reduction in the referral rate or a shift in the case-mix of referrals. It may be more realistic to expect liaison with GPs to facilitate the shared care of patients with severe mental illness and the early discharge of patients with less severe disorders.

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One hundred years ago

Temporary insanity

Recently the Brighton coroner referred to the automatic way in which the verdict of "suicide during temporary insanity" is given, and though we agree with him that this kindly verdict is too frequently given if the interests of truth only are to be served, yet it is not clear that any moral or social harm follows this sympathetic untruth. In the case under consideration a man who had attempted suicide had been brought up and tried before the assizes, and acquitted. Two doctors seem to have seen him, and to have decided that at that time he was not of unsound mind, yet the poor fellow, after being at home and being depressed for a fortnight, killed himself. The earlier stages of melancholia are generally free from delusions, and therefore would be considered by some medical men as uncertifiable. It will never be possible to stop all melancholiacs from self-destruction, and for their cure some risk must often be run, and generally the verdict of temporary insanity is justifiable in such cases.

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British Medical Journal, 20 March, 1897, 738.

Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Epsom, Surrey

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