(Indian group: 7.5%; British group: 35.5%, $P<0.05$) while phobias for sudden death (Indian group: 30%; British group: 10%, $P<0.05$) were more frequent in the Indian group. Associated somatic symptoms were significantly more frequent in the Indian sample, in keeping with earlier observations of the predominance of somatisation in non-western cultures (Carstairs & Kapur, 1976). Precipitating psychosocial stressors were more frequent in the Indian group (57.5%) as compared to the British group (40%; $P<0.05$). Family history of phobic illness was significantly less frequent in the Indian group (2.5%) as compared to the British group (9%; $P<0.05$).

Clearly, the clinical patterns of phobic neuroses in western and non-western clinic populations are not essentially similar as Drs Raguram and Bhide appear to conclude. Our data indicate important differences even after careful matching of the two groups. While these differences may indeed be due to a variety of psychosocial factors, more field studies are needed before venturing fanciful culture-based explorations.

M. S. KESHAVAN
V. K. YERAGANI
J. CHAMBERS

Lafayette Clinic
951 E. Lafayette
Detroit, Michigan 48207

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Neuroleptic Malignant Syndrome and Lethal Catatonia

DEAR SIR,

In their review of the neuroleptic malignant syndrome (*Journal*, January 1986, **148**, 47–51) Abbott and Loizou correctly point out that it is clinically identical to Stauder's lethal catatonia; however, in common with previous writers on this subject they do not suggest how the two conditions may be distinguished. Lethal catatonia has been recognised for over a century as a rare and dramatic cause of sudden death in mental patients, but in recent decades this diagnosis has suffered a curious eclipse. As described by the clinicians of the pre-neuroleptic era it typically presented with a prodromal phase of personality change, hyperactivity, affective disturbance, delusions, hallucinations, confusion and catatonia. Since the introduction of neuroleptic drugs in the 1950s, patients presenting with such florid psychotic symptoms will have received a major tranquillizer as a matter of course, and any subsequent hyperpyrexia may well have been attributed to the drug rather than the original disorder.

Is it then possible that all cases of neuroleptic malignant syndrome are in fact nothing more than the old lethal catatonia in spurious association with new and commonly-used drugs? The existing literature is not very helpful on this question: examination of published cases of neuroleptic malignant syndrome shows that many closely resemble the classic clinical picture of lethal catatonia (for example, the case described by Abbot and Loizou), but the uneven quality of description limits the conclusions that may be drawn by such comparisons (Peele & Von Loetzen 1973). Taken alone, however, these case reports cannot be regarded as adequate evidence for a separate neuroleptic-related condition. More convincing in this respect are descriptions of the syndrome in non-psychotic cases (Burke *et al*, 1981); cases where clinical course has been related to the kinetics of the implicated drug (Allan & White, 1972); and relapses of the condition following re-exposure to neuroleptics (Coons *et al*, 1982). Reports of typical cases in association with other dopamine-depleting drugs and with the withdrawal of dopamine enhancers such as levodopa also support the existence of a disorder secondary to iatrogenic disturbance of central dopaminergic transmission. However, it remains likely that the 'neuroleptic malignant syndrome' as we currently perceive it is a hybrid of this iatrogenic disorder and mis-diagnosed lethal catatonia.

If this clinical syndrome is indeed due to a disorder of dopaminergic function, then it is of some interest that one form of the disorder appears to have existed long before the introduction of major tranquillizers. In follow-up studies of the survivors of lethal catatonia there is a variable but persistant association with subsequent functional psychosis, usually described as schizophrenia (Arnold & Stepan, 1952). If the idiopathic form of this syndrome is associated with an increased risk of future schizophreniform psychosis, and the iatrogenic form with exposure to dopamine-blocking drugs, then the pre-neuroleptic accounts of lethal catatonia may represent important historical evidence in support of the dopaminergic theory of schizophrenia. This is an intriguing possibility and it deserves further study. However, it will first be necessary for us to

rediscover lethal catatonia, and to develop criteria for distinguishing the idiopathic from the iatrogenic.

JAMES LINDESAY

UMDS (Guy's Campus)
London Bridge, London SE1 9RT

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Lithium and Piroxicam

DEAR SIR,

Walbridge and Bazire (*Journal*, August 1985, **147**, 206–207) report an important interaction between lithium carbonate and piroxicam. In their discussion they seem to overlook the possibility of lithium toxicity having been precipitated by piroxicam further compromising the patient's already deteriorated renal function (creatinine clearance rate 51 and 55 ml/min on two occasions).

The consequences of prostaglandin inhibition by a non-steroidal anti-inflammatory drug (NSAID), such as piroxicam, on renal function in healthy subjects is controversial (Gullner *et al*, 1980). It is clear, however, that renal function is most likely to be adversely affected by a NSAID if it is already compromised (Sellars & Wilkinson, 1983). Prostaglandins become progressively more active with deteriorating renal failure (Calin, 1983). Renal prostaglandins (notably PGE2) are potent vasodilators of renal circulation. In experimental models of renal ischaemic stress, prostaglandin inhibition results in enhanced renal ischaemia since vasoconstriction is unopposed (Henrich, 1983).

The lithium toxicity may therefore have resulted from a sudden impairment of renal lithium excretion, mediated by prostaglandin inhibition by piroxicam.

R. K. SHELLEY

St Vincents Hospital
Elm Park
Dublin 4

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Schizophrenia with Good and Poor Outcome

DEAR SIR,

The studies by Kolakowska and her colleagues (*Journal*, March, 1985, **146**, 229–246 and April 1985, **146**, 348–357) illustrate the difficulty of obtaining longitudinal information from a cross-sectional study. The authors attempted to relate CT scans, cognitive impairment and neurological soft signs to outcome of schizophrenia, but did not carry out these investigations on initial presentation; in most cases these examinations appear to have been done at or near the end of the outcome period. The authors found that enlarged ventricles and cognitive impairment were associated with unfavourable outcome, and went on to suggest that "organic deficit may contribute to an unfavourable outcome". This ignores the possibility that some of the abnormalities found may have been at least in part consequent upon poor outcome of factors associated with it rather than predictors of it.

The study is weakened by the high rate of attrition; only 59 out of 118 patients satisfying their inclusion criteria actually participated in the study. The authors are aware of this problem and state that "the sample cannot be considered as representative of the population from which it was drawn". This does not appear to have deterred them from making sweeping generalisations about possible sub-types of schizophrenia.

In our opinion, the demonstration that the ratio of plasma drug concentrations to drug dose does not differ between the various outcome or response groups is not proof enough to eliminate all likelihood of pharmacological tolerance in the patients receiving fluphenazine or fluphenthixol who responded unsatisfactorily to these drugs. Information about the tubero-infundibular-dopaminergic axis obtained from plasma prolactin levels cannot be extrapolated to other regions of the brain such as the limbic or cortical areas (Thorner & Evans, 1984). It also leaves unanswered the question of plasma levels of psychoactive metabolites, and also the possibility of pharmacodynamic tolerance.