at the time of admission, the most suitable diagnosis might have been an acute psychotic episode.

If acute psychotic reactions occur in Africa and the West Indies, it is likely that they will be found in Britain in immigrants from those areas. 'Acute psychotic reaction' is not a favoured British diagnosis, and while some authors stress the presence of 'atypical reactions' among them, most suggest that psychoses in immigrants can be easily fitted into Kraepelinian categories (Copeland, 1968; Hemsi, 1967; Rwegellera, 1977). West Indian patients have been reported as having high rates of schizophrenia and low rates of affective illness compared to the British-born population (Cochrane, 1977).

A prospective study we have carried out in East London on a series of patients with religious and 'cultural' delusions yielded 24 African and Caribbean-born patients. A Religious Interest Questionnaire and the Present State Examination were used to interview the patients and their relatives. In the 16 patients without first-rank symptoms of schizophrenia (as defined by the PSE nuclear syndrome) a consistent clinical pattern emerged of an initially disturbed and acute onset with agitation, persecutory delusions involving witchcraft, and auditory hallucinations, in the absence of hypomanic affect or clouding of consciousness. These florid symptoms disappeared within a few days, to be replaced by depressive features such as loss of interest, loss of energy and difficulty in concentration, poor appetite, and in some patients depressed mood. There had been similar episodes, which had been diagnosed as schizophrenia, in 12 patients.

It seems possible that these patients resemble those diagnosed as having acute psychotic reactions in Africa and the Caribbean, and are similar to some of the patients from these areas diagnosed in Britain as being schizophrenic. If this is the case, the diagnoses appear to be largely based on the initial symptoms observed at the time of admission. A diagnosis made a few days later without reference to the state when first seen would perhaps be, more suitably, depression. Such patients could be described as experiencing acute psychotic reactions with later depressive features or essentially depressive illnesses with an initially agitated paranoid presentation.

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RISKS OF TRICYCLIC ANTIDEPRESSANTS

DEAR SIR,

In comparing the relative hazards of antidepressant treatment and death from suicide, Dr David Shaw (*Journal*, May 1977, **130**, pp 432–51) quotes figures from a recent paper by Girdwood (1) which show the number of deaths per million prescriptions to be 2·3 in the case of amitriptyline and 3·6 in the case of imipramine. Girdwood's paper, however, deals only with deaths which occurred at therapeutic doses. His figures exclude the much larger number of deaths due to deliberate over-dosage of tricyclic compounds.

As it happens, I can supply this figure. There were 8·1 million antidepressant prescriptions in 1974, of which about 95 per cent appear to have been tricyclic drugs. I have previously reported a method of calculating the number of fatal suicidal poisonings due to tricyclics which almost certainly gives a conservative estimate (2, 3). There were 167 such deaths in 1974, which means that there were at least 20 deaths per million tricyclic prescriptions. If *all* suicidal, accidental and undetermined deaths involving tricyclics are included, there were twice that number.

In any depressed patient the risk of suicide always exists, and it is therefore particularly important to avoid prescribing drugs with which the patient can easily kill himself. The tricyclics are the most toxic of the commonly prescribed psychotropic drugs (4).

Tricyclic overdose is more difficult to treat than barbiturate overdosage, and whereas barbiturate deaths have been declining over the last few years as a proportion of all suicidal poisonings the proportion of suicidal deaths due to tricyclic poisoning has been steadily increasing—from 1 per cent of all suicidal poisonings in 1965 to 9 per cent in 1974 (2, 3).

I am certainly not arguing that tricyclic drugs should be abandoned, but I do believe that their indiscriminate use, particularly but not exclusively in general practice, has probably caused more harm than it has alleviated. As Dr Shaw pointed out, there are now a number of non-tricyclic compounds which seem to be just as effective as the tricyclics, but have very much lower toxicity. It is my view that one or other of these drugs should now be the antidepressant of first choice in general practice and for the treatment of psychiatric out-patients whose medication cannot be reliably supervised. Tricyclics exemplify perfectly the adage that all drugs are dangerous but some are more dangerous than others.

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TRICYCLIC PLASMA LEVELS

DEAR SIR,

Dr Ziegler and his colleagues (*Journal*, August 1977, **131,** pp 168–71) reported that plasma levels of amitriptyline and nortriptyline after administration of amitriptyline hydrochloride as a single daily dose were comparable to those achieved with a thrice daily dosage schedule, and found total tricyclic levels decreased by a modest 23 per cent during the sampling period of 11 to 20 hours after the last single daily dose. Unfortunately, they used a similar sampling schedule to Braithwaite *et al* (1), and no plasma levels were measured during the 11 hours immediately following the single daily dose, the time when the most marked changes in plasma level might have been expected from a rapidly absorbed drug.

As part of a larger study, we have recently examined (*Neuropharmacology*, in press) between-dose plasma level profiles of nortriptyline in the same subjects after receiving either a three-times-daily nortriptyline preparation (10 mg nortriptyline, 0·5 mg fluphenazine) or a once-daily preparation (30 mg nortriptyline, 1·5 mg fluphenazine). With each preparation the plasma level studies were carried out after seven days medication, and samples were obtained just before and during the 8 hours following the once-daily dose and the first dose of the thrice-daily regimen. Although the two preparations gave similar before-dose plasma nortriptyline levels in the individuals studied, once-daily dosing produced a slow peaking effect in five out of six subjects which was not evident on the three-times-daily regimen. In two subjects the nortriptyline concentration increased after four hours to a maximum of 300 per cent of the pre-dose concentration.

Fluctuations of this magnitude suggest there could be important therapeutic differences between once-daily and divided dose regimens of the same rapidly absorbed drug. Thus lower than customary doses of tricyclic antidepressant, if given once-daily, may be adequate for many patients since peak plasma concentrations within the recommended steady-state therapeutic range of 50–150 ng per ml (2) may be sufficient to produce a satisfactory antidepressant effect. This would avoid the risk of a poor response, as well as toxicity, associated with the high steady-state plasma concentrations which Montgomery *et al* (3) found in 61 per cent of their patients on standard doses of nortriptyline.

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