change from pre-treatment scores was small, the majority of the patients showing little or no overall improvement. We concluded that although d-propranolol has a detectable therapeutic effect on schizophrenic symptomatology, this effect is more of pharmacological interest than of major clinical significance, as the change on rating scales did not compare favourably with the changes observed with conventional neuroleptics in adequate doses.

Propranolol has been a subject of research for over a decade, and several studies conclude that it has a statistically significant effect in reducing psychotic symptomatology. Clinicians are far from convinced. A weak antipsychotic effect for propranolol is the best that can be concluded from experience so far. It remains to be seen whether or not the propranolol molecule can be modified to produce a more effective antipsychotic agent. The clinical investigator has done his work and this is now a challenge for the pharmaceutical industry.

RAHUL MANCHANDA

University of Western Ontario
St Thomas Psychiatric Hospital
St Thomas, Ontario, Canada N5P 3V9

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Professor Eccleston and Dr Hassanyeh Reply

SIR: Dr Manchanda asks if a statistically significant finding should also be seen as clinically significant. He concludes that with propranolol in schizophrenia (despite several studies which suggest a useful contribution) clinicians would regard such a finding, based on statistical significance, unconvincing. It is axiomatic that progress in research must be based on scientific methodology including statistics. If we revert to clinical opinion only, little progress in psychiatry can be hoped for. This, of course, does not mean that the findings of a study must be seen as clinically binding.

Dr Manchanda asks whether a dose of 400 mg thioridazine was therapeutically adequate. This is a relevant question, and further studies exploring this are obviously required. Our study, however, clearly suggests that propranolol at a dose of 640 mg a day was superior to thioridazine at a dose of 400 mg a day in patients with chronic schizophrenia. This superiority is based on the statistical findings in relation to measures on the BPRS (total score, positive and negative symptoms) and on the NOSIE. It should be noted also that although the improvement was not large there was a variation between the patients, some doing much better than others—but not in such a way that one could predict who was likely to show most benefit.

We do not suggest that propranolol radically changed or cured the illness—tables III and IV of our paper attest to that. What we do suggest is that it reduced the severity of some of the positive and negative symptoms; i.e. it made a quantitative and not a qualitative impact on the illness. Our conclusions were that propranolol at 640 mg/day may have a useful part to play in the treatment of chronic schizophrenia but that thioridazine at 400 mg/day does not. We also suggested that propranolol's effects on the negative symptoms warranted further investigation.

Would a higher dose of thioridazine have been more efficacious? As indicated earlier, this needs to be tested out in a clinical trial. Our impressions, however, are that it would not. Pre-trial, virtually all patients, whether in the propranolol or thioridazine group, were on *both* a depot and an oral neuroleptic at doses which clinicians would not have regarded as sub-optimal, yet despite which their illness had shown little or no change. If in this group of patients propranolol was shown to be beneficial, as was shown in our study (if only in a quantitative sense), what we suggested was that it ought at least to merit consideration in the drugs available to us which could be used in this condition.

DONALD ECCLESTON
FUAD HASSANYEH

The Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne NE1 4LP

Is there a Right-hemisphere Dysfunction in Asperger's Syndrome?

SIR: We read with interest the report on a case of Asperger's syndrome (*Journal*, November 1985, **147**, 566–509), an entity unknown to us. We were surprised to see that one of the main features was non-verbal communication disorder (the inability to perceive the meaning of expressions and gestures of others and a poverty of non-verbal expressions), which has been named global aprosodia by Ross (1981) and is caused by right-hemisphere damage. The discrepancy between verbal and performance IQ in this patient also suggests right-hemisphere

damage, as the authors pointed out. Wing (1981) reviewed six cases of Asperger's syndrome. Five of her six patients did the WAIS or WISC tests; in four of them the verbal IQ was higher than the performance IQ (being quite a bit higher in two of them).

Weintraub & Mesulam (1983) described 14 patients with right-hemisphere dysfunctions; as Denckla (1983) points out, they resembled those with Asperger's syndrome. The Weintraub & Mesulam patients had five features (introversion, poor social perception, chronic emotional difficulties, inability to display affect, and impairment of visuospatial representation); Asperger's syndrome patients show four of these (Wing, 1981).

Weintraub & Mesulam (1983) found a history of neurological disorders (infantile hemiplegia, perinatal stress and seizures) in 10 patients, and three of the remaining four had an abnormal family history. Wing (1981) described a history of cerebral damage in some patients, and found that parents' behaviour often resembled their childrens'.

These facts suggest that both groups of patients, those with Asperger's syndrome and those of Weintraub & Mesulam, are rather similar or share some characteristics. Perhaps the problem is inadequate communication between neurology and psychiatry. Weintraub & Mesulam emphasize right-hemisphere dysfunction but interpersonal aspects are stressed in Asperger's syndrome.

J. de LEON MOLINA

C. E. Ramon y Cajal
Madrid, Spain

J. MUÑOZ RUATA
E. PICO SOLER

C. E. V. de Lourdes
Majadahonda, Spain

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Depression in General Practice

SIR: In their valuable study of the clinical features of depression in general practice and comparison with out-patients, Sireling *et al* (*Journal*, August 1985, **147**, 113–119) state: "Important factors associated with psychiatric referral appear to be severity and chronicity of the depression. This contrasts with Fahy's findings that neither factor played a major part, although both might be expected to do so".

Neither of these statements is completely accurate. First, Sireling *et al* (1985) did not study the psychiatric referral process. They compared general practice (GP) depressives (recognised and not recognised, etc.) with a separate group of depressed out-patients. This procedure does not justify conclusions—however correct these may later turn out to be—about factors affecting the process of referral. Secondly, my study (Fahy, 1974) was a prospective study of GP-identified depressives specifically designed to show how referrals differed from non-referred depressives from amongst a defined general practice population at risk. Subsequent reports of the findings made it clear that by every usual criterion of severity of illness (rating scales, weight of symptoms, factor scores, etc.) referred depressives were more severely ill and more endogenous. However, Sireling *et al* appear to have been misled by one set of multiple regression data (Table II in the paper in question) which showed that 'severity' and 'duration over one year' were statistically outweighed as predictors of referral by five other features, notably 'hopeless'. They appear not to have noticed that 'severity' was rated not by the research psychiatrist but by the eight collaborating GPs whose reliability was not measured.

The failure of these two features to emerge as superior predictors of referral does not mean they are of no value for this purpose in practice. The arithmetic of regression analysis assigns a weight to each variable expressing the individual predictive power of that variable when relationships with all other variables have been taken into account. The relatively minor roles of 'severity' and 'duration over one year' mean that it is unnecessary to invoke these variables in prediction of referral because of the greater importance of other clinical features which are themselves correlated with either severity or chronicity or both. In fact, the combined predictive power for referral of both 'severity' and 'duration over one year' was 14.4% of the total predictive value of the eight features considered in this particular analysis. Far from being "in contrast" with my data, Sireling *et al's* observations in this context are quite consistent with mine despite differences in material and method and an interval of more than ten years between the two studies.

Concepts of severity and of chronicity are difficult to define precisely in community settings. Total rating scale scores, symptom counts, weighted scores on dimensions, time off work etc. are just