The treatment of schizophrenic patients with drugs is not without controversy. There is little doubt that a way to check violent and deranged outbursts quickly and dependably has provided a sense of security for those involved in day-to-day caring for patients. The means to control socially disruptive behaviour has permitted more humane conditions for treatment. Through drugs patients have become accessible to refined non-pharmacological approaches such as dietary programmes and psychotherapies. However, the benefits of antipsychotic drugs go hand in hand with undesirable effects, notably parkinsonian tremors. To tranquillize mood or behaviour may be to lose vitality and blunt the experience of happiness and joy. More serious side effects are those like oro-facial dyskinesias which may be irreversible, continuing after the drug is withdrawn.

From another standpoint, drug therapy has advanced our understanding of the pathogenesis of schizophrenia. Research with animals has shown that most antipsychotic drugs reduce dopamine transmission (Carlsson and Linqvist, 1963; Crow et al., 1976; Hornykiewicz, 1966; Iverson, 1975; Matthysee, 1973; Seeman and Lee, 1975; Seeman et al., 1976; Snyder et al., 1974). A blocking of dopamine in the brain's limbic regions is thought to reduce psychotic behaviour, while undesirable Parkinsonian effects stem from blocking dopamine synapses in striatal regions. Treatment may be advanced when this knowledge is further refined and when drugs are found to act more selectively on the brain mechanisms responsible for psychosis.

The present report concerns research with one of a class of drugs new to the treatment of schizophrenia. Preliminary observations and now objective, controlled evidence indicate that while sharing the benefits of conventional treatment fewer disadvantages have been encountered and additional benefits may accrue.

Like many scientific discoveries the application to psychosis of the drug in question was accidental. In a case of porphyria accompanied by rapid pulse rate and florid psychotic symptoms the pulse returned to normal and psychosis disappeared after propranolol, a drug known to lower pulse rate, was given in what was at the time a high dose (Atsmon and Blum, 1970). Subsequently propranolol treatment was examined in seven acute and five chronic cases of schizophrenia. Little success was found in chronic patients but five of the acute cases were considered 'much improved'. Improvement was associated with high urinary catecholamine levels, particularly MHPG.
Later 13 excited and emotionally labile cases with acute psychotic episodes were found to improve or lose all symptoms on propranolol, some within 24 hours (Atsmon et al., 1972). In another study ten cases of post-partum psychosis were administered either propranolol or chlorpromazine. Those on propranolol were discharged on average in 61 days compared with 104 days (perhaps an unusually long time) on chlorpromazine. With propranolol there was noticeable improvement after 3 days compared with 55 days on chlorpromazine (Steiner et al., 1973).

Two investigations followed in which the drug was administered to schizophrenic patients with little success. In one, eight patients who had been resistant to treatment for a year were examined on conventional medication which was then withdrawn and replaced first with placebo for 4 weeks and then propranolol for between 6 and 10 weeks in daily doses up to 720 mg. While most patients were reported as calmer on propranolol the drug had no reliable antipsychotic effects (Gardos et al., 1973). In the second investigation three compounds were tried: (1) propranolol in its racemic form ((±)-propranolol) as used by other investigators; (2) the dextro isomer (+)-propranolol which has less of the hypotensive effects of the racemic form; (3) oxprenolol, a drug of the same class of β-adrenergic blocking agents. These were administered to cases of schizophrenia, mania and organic psychosis. The two cases of organic psychosis and two/four cases of mania who completed the course of treatment were noticeably improved on ±-propranolol. In six cases of schizoaffective psychosis there was slight improvement and in three cases of schizophrenia no improvement (Racknesperger et al., 1974; Van Zerssen, 1976).

The equivocal nature of the results apart, the early applications of the drug encountered drawbacks in the form of toxic side effects. Fortunately, subsequent studies in Britain with 55 cases of florid schizophrenia showed that toxic effects could be avoided by increasing dose in a more gradual fashion. Excessive and possibly toxic doses were also avoided by withholding increments in dose at signs of impending toxicity or clinical improvement (Yorkston et al., 1976b). With this regimen lower doses of the drug were effective about 1-0 g compared with 2-4 g used by others. In 28 of the 55 cases florid symptoms remitted at least temporarily and others showed some improvement. Improvement and loss of all symptoms were found with chronic as well as acute cases, some of whom lost all schizophrenic symptoms after more than 20 years illness. In some chronic cases remission of symptoms took as long as a year, indicating that it was worth persisting with treatment even when in the early stages there was minimal improvement (Yorkston et al., 1974; Yorkston et al., 1976a).

With a safe method for administering propranolol a controlled study with cases of chronic schizophrenia was conducted in which either propranolol or a matching placebo of identical appearance and taste were added to conventional neuroleptic medication. Results with the first 14 cases have now been analysed and published (Yorkston et al., 1977). This was the first controlled study of the efficacy of propranolol in treating schizophrenia. Details of the patient sample are shown in Table 1.