Differential Effects of Chlordiazepoxide and Fluphenazine in Two Anxious Patient Populations*

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Introduction

It is quite evident from the literature that results reported in clinical evaluations of psychopharmacological agents are far from uniform. Not only specific drug effects but a number of non-specific or non-drug factors (Rickels, 1965a), including differences in patient populations (Uhlenhuth et al., 1966), have been indicated as significant factors for clinical outcome of drug therapy. Because of the latter observation, we have carried out several double-blind clinical trials simultaneously with low socio-economic clinic and higher socio-economic general practice patients, in a further attempt to elucidate causes for differences in drug responses between different study populations.

In 2 recently published studies we could demonstrate that private practice research is indeed feasible, that methodological problems can be dealt with, that high research standards can be achieved through appropriate physician training, and that meaningful and reliable data can be collected (Rickels et al., 1964a, 1966).

The present study was conducted simultaneously in the medical clinic of the Philadelphia General Hospital (PGH) and in the offices of 4 General Practitioners (G.P.) in private practices. It was designed in an attempt to test for the effect of population differences, particularly differences in social class on clinical improvement and on the reporting of side reactions. A design was chosen which allowed to test for drug effects, population effects, and drug × population interaction effects.

Based on our prior clinical experience we hypothesized that 1. higher socio-economic general practice patients would be more disturbed by

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sedative side effects, while lower socio-economic patients would be more disturbed by autonomic or "other than sedative" side effects and 2. fluphenazine with its mild extrapyramidal side effects, which some patients may interpret as stimulation, would be least liked by the low socio-economic, more somatically oriented medical clinic patients, resulting in less clinical improvement than produced by chlordiazepoxide in the same patient group or by fluphenazine in the general practice group. No prediction for a differential population response to chlordiazepoxide was made. Similar effects of a differential side reaction interpretation on clinical outcome was reported earlier by this group in a double-blind evaluation of Deprol, a combination of meprobamate and benactyzine, and imipramine (Rickels et al., 1964b).

**Method**

**Population**

The study population consisted of neurotic outpatients from the medical clinic of a large city hospital and from private general practice. They suffered predominantly from anxiety and somatic symptoms of psychogenic origin. Patients with psychosis, organic brain syndrome, alcoholism, and sociopathic personalities were excluded. Mild degrees of depression did not disqualify patients from this study, as long as anxiety was the predominant complaint. Sixty-six patients were diagnosed as "neurotic anxiety reaction", 37 patients as "mixed neurotic reaction", and the remainder as "conversion reactions, obsessive-compulsive reactions", or "psychophysiological reactions". No population differences existed in diagnosis.

As was anticipated, both population groups differed significantly in several demographic variables, primarily in areas related to social class and its accompanying social adjustment and social stability (Table 1). Private general practice (G.P.) patients were primarily white, better educated, had higher occupations, came from more stable families with less divorces and separations, and were more frequently aware that they had emotional problems. According to Hollingshead and Redlich, they were primarily of lower middle socio-economic status (Class III), while clinic patients were of lowest socio-economic status (Class V) (Hollingshead).

General practice patients were less drug pretreated, realized more clearly that they had emotional problems, and were considered by their physicians to respond best to a combination of drugs and some form of psychotherapy, but not drug therapy alone. Interestingly, and also possibly reflecting difference in social class (Stunkard, 1966), is the greater concern for weight control observed in the general practice patients (8 patients versus 1 patient took diet pills). General practice patients also drank significantly more coffee than did clinic patients ($p < .01$).