Imipramine in Preschool Autistic and Schizophrenic Children

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Imipramine was studied in 10 autistic and schizophrenic children 2 to 6 years of age, whose intellectual functioning ranged from low average and mild to severe mental retardation. The purpose of this pilot study was to explore the effects of imipramine in this patient population. Imipramine showed a mixture of stimulating, tranquilizing, and disorganizing effects. Three children improved markedly, 3 slightly, and 5 became worse (nonblind evaluations). Only 2 were rated improved by the "blind" psychiatrist. In general, this was not a good drug for this group of children. The overall effect was infrequently therapeutic and usually outweighed by the toxic effects. Epileptogenic effect, effect on psychosis, as well as possible mechanisms of action of imipramine are discussed. It is suggested that this drug merits further exploration in the most retarded, mute, anergic children, and in those with only borderline or little psychotic symptomatology.

This pilot study represents a part of an ongoing research program in psychopharmacology for schizophrenic children, under 6 years of age, a group which is most resistant to any available treatment (Fish, 1960, 1964, 1968; Fish, Shapiro, & Campbell, 1966; Fish, Shapiro, Campbell, & Wile, 1968). Aside from their psychosis, the children function on a retarded level, their development is uneven and delayed, and much of their behavior, such as language and performance, is rudimentary or absent. They are withdrawn, and in a great many of them apathy, anergy, dreaminess, and distractibility as well as reduction of motor activity and initiation are prominent features.

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In the earliest years drug therapy is an essential part of the total treatment. These children, however, pose a problem even in this respect. They may be excessively sedated by small doses of chlorpromazine. The less sedative neuroleptics, such as trifluoperazine (Fish, 1960; Fish et al., 1966, 1968) and trifluoperidol (Fish, Campbell, Shapiro, & Floyd, 1969a) yield somewhat better responses. In our experience, of all neuroleptics, the children were most responsive to thiothixene (Campbell, Fish, Shapiro, & Floyd, 1970) and molindone (Campbell, Fish, Shapiro, & Floyd, 1971). Although chemically unrelated, both have some stimulating effects on behavior. Thus, the less sedative neuroleptics were more effective than the more sedative ones for this group, since sedation often resulted in decreased functioning (Fish, 1960; Fish et al., 1966, 1968, 1969a; Campbell et al., 1970).

In view of the above, it seemed to us that an antidepressant which had stimulating as well as tranquilizing properties could be useful for this young patient population.

Imipramine, a potent antidepressant, has been used since the 1950s. Studies in adults showed that depressed patients with psychomotor retardation respond better to imipramine than those who are agitated (Kuhn, 1958; Overall, Hollister, Johnson, & Pennington, 1965). Imipramine was also found to be superior to thioridazine in reducing motor retardation (Overall, Galveston, Hollister, Meyer, Kimbell, & Shelton, 1964) and to chlorpromazine (Raskin, Schulerbrandt, Reatig, Chase, & McKeon, 1970). This was of interest to us, since many patients in our population are anergic and hypoactive and become excessively sedated by chlorpromazine.

From the early reports of imipramine in disturbed children, as well as from studies on its effects on enuresis, it was hard, if not impossible, to evaluate the drug's therapeutic effectiveness for childhood schizophrenia. The diagnostic categories were ill-defined and the age groups were not separated, even in many of the controlled studies on enuretics. However, some anecdotal reports on individual children suggested possible useful effects for our patient group.

In 1961, Crot reported the results of a preliminary investigation of imipramine in patients 9 to 18 years of age. His was not a homogeneous group for it included character disorders, reactive depressed states, neurotic depressions, and withdrawn, depressed mentally retarded children. Crot reported that his patients responded well to this drug; they became more attentive and were able to concentrate better. Seven cases in that group resembled our patients; these were the withdrawn, mentally retarded children with apathy, psychomotor retardation, distractibility, and short attention span.