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Clinical Experiences with Thioproperazine ("Majeptil")
in Chronic Schizophrenia, Psychotic Excitation,
and Senile Agitation

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Introduction

Thioproperazine is one of the more recent phenothiazine derivatives to be synthesised in the laboratories of Rhône-Poulenc in France. Chemically it resembles prochlorperazine, differing only in that the chlorine atom has been replaced by a dimethylsulphamoyl group. Pharmacologically it is shown to possess anti-emetic properties and cataleptic activity 50 times and 10 times respectively greater than prochlorperazine; but weaker effect on the autonomic system and on the production of hypothermia; while sedative properties are very low. The acute toxicity (in mice by the oral route) is less than half that of chlorpromazine (COURVOISIER et al. 1958).

As might be expected from a drug with so marked cataleptic properties pharmacologically, thioproperazine was soon found to produce very marked neurological symptoms in patients. DELAY et al. (1958, 1959, DELAY and DENKIER 1961), as well as DENHAM and CARRICK (1961), have given thorough descriptions of the different clinical syndromes, neurological as well as psychological, which may be provoked by thioproperazine, especially when the discontinuous method of treatment is used (see below). Characteristic neurological syndromes are: the akinetic syndrome, with lethargy, apathy, bradykinesia, but without hypertonia; the hyperkinetic syndromes, with excitomotor, or dyskinetic, crises of different types; the akineto-hypertonic syndrome, with a parkinson-type rigidity as the most characteristic feature; and the hyperkineto-hypertonic syndrome, brought about by the association of an increasing hypertonia with an incessant desire for movement. These syndromes often occur in the succession stated. Concomitant with these neurological syndromes may be seen different psychological syndromes: the syndrome of indifference; anxiety reactions; variations of the thymic state; and the impatience malaise (DELAY et al. 1959). Autonomic disturbances, like severe sweating, excudation of sebum, and sialorrhea, are also frequently seen.
Thioproperazine may be given continuously, as are usually other neuroleptics; however, many investigators favour the discontinuous method of treatment, as outlined by Delay et al. (1958, 1959), with rapid increase of dosage until the appearance of certain neurological symptoms, e.g., rigidity, followed by abrupt withdrawal of the drug after giving this optimum dose for, e.g., five days. Many courses may be given if necessary, a lower maintenance dose usually being given to stabilize the effect obtained. With this treatment procedure, Delay et al. (1959) obtained many remarkable ameliorations notably in chronic or resistive schizophrenics and states of excitation and agitation. Perrin et al. (1958), also stressing the desirability of brief discontinuous courses, found that thioproperazine in schizophrenic and confusional states often shows a much more rapid, intense, and obvious action than is displayed by other known phenothiazines. Denham and Carrick (1961), employing the discontinuous treatment, and following up an average of 3 courses with a low maintenance dosage, achieved 32 total remissions out of 58 schizophrenics most of whom were chronic cases which had failed to benefit from earlier treatment. The discontinuous treatment has been used successfully in schizophrenics also by, among others, Van der Spek (1962) and Jacob et al. (1962), whereas far less satisfactory results have been reported by Ekholm et al. (1961) and Ollendorff (1962).

Some authors prefer to give the drug continuously, if necessary associated with an antiparkinson drug. Maurel et al. (1960), using mainly the continuous method, found that in chronic psychotics the therapeutic effect of thioproperazine is less constant, but quantitatively better than that of prochlorperazine; they think no other neuroleptic has to the same degree the power to transform the clinical appearance of chronic delusional psychoses or of resistant chronic schizophrenics. Rebêillard et al. (1961), also preferring to give the drug continuously, associated with an antiparkinson drug and another phenothiazine derivative to combat anxiety and insomnia, obtained varying degrees of improvement in 59 out of 72 schizophrenics. A combination of thioproperazine, trihexyphenidyl, and chlorpromazine—the latter being administered 6 days prior to as well as concomitant with the other drugs—has been used by Rigel et al. (1962), who found this method to be almost devoid of neurological side effects. Favourable results were obtained in about 80% of 54 cases. Rudrauf and Chalou (1961) found that the neurological side effects could be effectively controlled by orphenadrine, with no lessening of the therapeutic effect of the drug.

In the treatment of mania, results have been more consistent than in the case of schizophrenia. Very favourable results (however, usually on very small materials) have been reported by Delay et al. (1959), Perrin et al. (1958), Rebêillard et al. (1961), Ekholm et al. (1961), Ban et al.