Neuroleptic Plasma Levels and Tardive Dyskinesia

To the Editor:

Although Dr. Nasrallah's hypothesis (Neuroleptic plasma levels and tardive dyskinesia: A possible link? Schizophrenia Bulletin, 6:4-7, 1980) about the link of tardive dyskinesia to intermittent blood levels of neuroleptics is of interest, he appears to have confounded two aspects of this problem. First of all, he speculates that tardive dyskinesia may be more prone to develop in patients with marked variation in blood levels of neuroleptics. This confuses the population of patients with supersensitive dopamine receptors with the identification of these patients. Work to date has indicated that it is the chronic blockade of dopamine receptors that leads to increased dopamine receptor proliferation and hence supersensitivity (Baldessarini and Tarsy 1978). This is indicated by animal studies using not only behavioral measures (Gianutsos and Moore 1977; Moller-Nielsen et al. 1974; Tarsy and Baldessarini 1974) but also neurophysiologic (Yarbrough 1975) and biochemical measures (Muller and Seeman 1977). It is thus likely that patients who show lower levels of neuroleptics in their blood, whether through increased metabolism or decreased drug ingestion, manifest symptoms of tardive dyskinesia that have been already produced by chronic neuroleptic treatment.

Dr. Nasrallah's hypothesis is speculative and not supported by accepted basic neuroscience data, which indicate that chronic stimulation results in sub sensitivity and decreased stimulation supersensitivity as, for example, in denervation. This hypothesis would argue against the use of drug holidays, which, by providing the receptors with interaction with the agonist, allow for partial amelioration of the blockade of receptors that may result in receptor supersensitivity.

References


Tarsy, D., and Baldessarini, R.J. Behavioural supersensitivity to apomorphine following chronic treatment with drugs which interfere with the synaptic function of catecholamines. Neuropharmacology, 13:927–940, 1974.


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The Author Replies:

A large body of evidence exists, both in humans and in animals, that chronic dopamine receptor blockade by neuroleptic drugs (chemical denervation) results in dopamine re-