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Response

To the Editor:

We appreciate the comments of Growdon (1986) regarding our disappointing results with phosphatidylcholine (PC) in the treatment of tardive dyskinesia (TD). This neuroleptic-induced syndrome is of such importance that any potential treatment needs a thorough analysis before it is discarded as either practically or theoretically not useful. Growdon is correct that we presented mean data (Domino et al. 1985), and therefore, individual patient differences were not emphasized. As others have observed, we also had individual TD patients who improved. However, one of our most dramatic improvements occurred in a Lafayette Clinic patient who received only placebo and no PC. Hence, we decided to emphasize the group mean data on PC, which, in general, did not differ from the mean data on placebo using a double-blind experimental design.

Growdon feels that our findings differ from those of most published reports and that PC is the drug of choice for TD; he cites a review by Schiefe and Growdon (1982) on the treatment of TD. That review includes open studies in estimates of efficacy of PC, but does not include three recent double-blind studies (Perez-Cruet et al. 1981; Anderson et al. 1982; Jeste and Wyatt 1982a). In our paper, we listed all the double-blind studies that have been published so far on PC for TD. Excluding our own study, these involve a total of 28 PC-treated patients, 18 of whom failed to improve. Therefore, we cannot agree with Growdon that our findings markedly differ from other published reports. Other investigators who have reviewed the literature on the treatment of TD do not conclude that PC is the treatment of choice (Jeste and Wyatt 1982b; Casey 1985). In our opinion, at the present time, there is no satisfactory treatment of TD.

Among the double-blind studies with PC, improvement of TD occurred only in the two studies in which neuroleptic maintenance treatment had been withdrawn (Jackson et al. 1979; Perez-Cruet et al. 1981). This suggests that improvement may have been due to spontaneous recovery from withdrawal dyskinesia rather than to PC. Future studies must take into account TD patients who spontaneously recover following neuroleptic withdrawal over a prolonged period of time (years), as opposed to those TD patients who are maintained on neuroleptic medication. It should be emphasized that our TD patients continued to be on psychotropic drugs, because their psychiatric condition would not ethically allow drug withdrawal.

Growdon correctly points out that the rate of neuronal firing appears to determine the extent to which cholinergic neurons are sensitive to precursor availability. If TD patients have supersensitive dopamine receptors on their striatal cholinergic neurons, such neurons would have a lower firing rate, making them unlikely to take advantage of any increases in available choline. Theoretically, PC is less important as a precursor of acetylcholine in a cholinergic neuron whose firing rate is further diminished by an over-

active dopaminergic system. As neurotransmitter turnover best reflects overall cholinergic function, it is important to note that elevated choline levels have not been shown in animal studies to alter acetylcholine turnover in normally functioning cholinergic neurons (Eckernas et al. 1977; Brunello et al. 1982). Hence, we remain convinced that, unfortunately, PC is an ineffective treatment of TD both on a theoretical as well as a practical basis. For the benefit of all TD patients, nothing would please us more than to have future studies prove us wrong.

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Zinc and Childhood Hyperactivity

To the Editor:

It is well known that complications of pregnancy increase the risk of defective offspring, but specific correlations are more difficult to prove. There are some indications that zinc deficiency in pregnancy and pre-eclampsia may contribute to production of the hyperactive syndrome in progeny. Low zinc occurs consistently in severe pre-eclampsia (Hahn and Fuchs 1974; Brophy et al. 1985). Zinc deficiency is known to lead to a hyperactive syndrome in rats (Halas and Sandstead 1975). Childhood hyperactivity has been retrospectively associated with pre-eclampsia by Pasamanick and coworkers (Rogers et al. 1955). Table 1 gives results of our statistical power analysis (Thomas and Gart 1977) of the association of hypertension in pregnancy to syndromes associated with perinatal complications according to these authors (Rogers et al. 1955; Pasamanick and Knobloch 1961). Our statistical analysis of their data relating the incidence of hypertension in pregnancy in cases with a designated childhood disorder as compared to controls suggests that reading disorders and hyperactivity may be relatively more frequent than other negative outcomes. Their data do not support an association of mental retardation with pre-eclampsia.

The above would suggest that there may be analogous zinc deficiencies during development both in the hyperactive but previously zinc-deficient rat and