represent exaggerated vestibular sensation activated along with the autonomic dysfunction seen in mania.

Twenty-nine patients reported draining, fullness, or pain in the paranasal sinuses. Of these, 21 were using sympathomimetic preparations that can aggravate or precipitate manic episodes. Characteristically, these patients were intensely dysphoric and specifically fearful of stopping their sinus medications. Typically, the use of lithium to control the mania also controlled the sinus symptoms, after which the aggravating medication could be removed.

The prominence of these physical symptoms along with mania can distract the patient and physician from initiating the use of lithium salts and other treatment for mania. The usual and typical course is that the physical symptoms promptly remit as the mania comes under control with specific treatment. In a considerable fraction of the cases I have described, distraction of care toward attempts to relieve the physical symptoms had delayed commencement of specific treatment for mania.

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## Use of Unproven and Unapproved Drugs to Treat Cocaine Addiction

SIR: Although there have been reports (1, 2) of desipramine's *statistically* significant efficacy in the outpatient treatment of cocaine addicts, other investigators (3, and unpublished manuscript by I. Arndt et al., 1989) have found no differences between desipramine and placebo with respect to patients' craving for cocaine, retention of patients in treatment, and their use of cocaine during treatment. More importantly clinically, desipramine has not been demonstrated to improve retention of patients in outpatient treatment or decrease rates of relapse. Thus, *clinically* significant efficacy of desipramine in the treatment of cocaine addiction has not yet been demonstrated. Moreover, although there have been no reports of cardiovascular problems by cocaine addicts receiving desipramine in controlled studies, tricyclic antidepressant medications may affect cardiovascular function by causing postural hypotension or slowing cardiac conduction (4).

Given that desipramine is approved and available for treatment of depressive syndromes, precautions are advised for physicians who prescribe desipramine or other as yet unproven medications (e.g., imipramine, carbamazepine, and amantadine) for cocaine addicts without the symptoms and clinical course of a major depressive syndrome or other conditions for which a drug is approved. In these situations one may wish to use measures similar to those used by clinical researchers testing an investigational drug: writing a treatment protocol, having the protocol reviewed and approved by an institutional review board, and using informed consent procedures which state to prospective volunteer patients that the drug is so far unproven for treatment of cocaine addiction and which list possible adverse reactions.

Further research on desipramine and other pharmacological agents is needed in order to better determine their efficacy in the treatment of cocaine addiction, which is presently an important public health problem.

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## Effects of Sedatives and Neuroleptics

SIR: I found "Time Course of Antipsychotic Effects of Neuroleptic Drugs" by Paul E. Keck, Jr., M.D., et al. (1) to be a blockbuster. It is the first anti-antipsychotic article I've seen in many years.

There is a seeming contradiction: "The efficacy of neuroleptics . . . has been established beyond doubt" versus "The same overall degree of improvement was observed . . . with all the agents tested" and "When a neuroleptic was compared to a sedative . . . the sedative demonstrated efficacy similar to that of the neuroleptic during the first day . . . and through 4 weeks . . . of treatment."

Many questions arise in this admittedly naive clinician. Has our clinical judgment about the efficacy of antipsychotics been a fixed, encapsulated, delusional perception, systematized by the dopamine hypothesis? What are the implications for the dopamine hypothesis? If there is no difference in outcome in a month, how about 2 months, or 6, or a year, or a lifetime? Do sedatives prevent relapse as well as antipsychotics do? Are we back to square 1 in antipsychotic psychopharmacology?

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## Decisions in Psychopharmacologic Treatment

SIR: I was immediately taken by the letter from Lakshmi N. Yatham and associates (1). Although the intent of the letter was clearly to raise interest in exploring the safety and efficacy of combining carbamazepine with monoamine oxidase inhibitors (MAOIs), I believe the letter raises a far mor