drops from neurologic disease, pilocarpine, a parasympathomimetic agent, is safe and reliable. It causes constriction of the iris sphincter unless atropine or another postsynaptic blocker, such as tropicamide, the substance involved in this case, has been used.

Physostigmine salicylate (Antilirium) was not used, but it is effective in treating anticholinergic intoxication when administered intramuscularly (1 mg repeated in 15–20 minutes if necessary).

In Ms. A's case, the anticholinergic effects of chlorpromazine, amitriptyline, scopolamine (Sominex) (10), and tropicamide were probably additive.

Although her disorientation cleared rapidly, Ms. A maintained that her hallucinations persisted during her 2-week hospitalization. However, it is difficult to know whether this was actually the case. Given the previous diagnosis of Munchausen syndrome and her unusual willingness to assume the psychiatric patient role as well as the medical-surgical patient role, it is not unlikely that she was attempting to prolong her hospitalization.

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Neuroleptic-Induced Supersensitivity Psychosis

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Dopamine receptor binding sites have been reported to increase in the neostriatum after chronic treatment with neuroleptics, which could account for the dopamine hypersensitivity that induces tardive dyskinesia (1). We propose that similar changes may occur in the mesolimbic region in response to the chronic dopamine blockade of these drugs. Three kinds of clinical evidence are compatible with this hypothesis: 1) central nervous system (CNS) drug tolerance; 2) psychosis following neuroleptic withdrawal, which is correlated with signs of dopamine supersensitivity and which we would therefore term "supersensitivity psychosis"; and 3) psychosis associated with a sudden decrease in prolactin levels following neuroleptic withdrawal.

Study Reports

CNS drug tolerance. In a double-blind controlled study we compared fluphenazine enanthate given every 2 weeks with fluphenazine decanoate given every 4 weeks in the maintenance treatment of 48 schizophrenic outpatients (2). Before entering the trial, patients had received fluphenazine enanthate routinely for periods of 1 to 42 months (median=14). All patients underwent a further 1-month period of stabilization with fluphenazine enanthate. The bimonthly dosages of the fluphenazine enanthate-treated patients on entering the trial ranged from 2.5 to 125 mg (median=25 mg, mean=39.3 mg) and after 7 months of treatment ranged from 2.5 to 325 mg (median=50 mg, mean=69.1 mg). Thus, substantial increases in dosage were required to maintain the mean therapeutic effect at the same level. In animal studies, prolonged exposure to neuroleptics leads to increased dosage requirements to block the behavioral effects of apomorphine (3, 4).

Psychosis associated with signs of dopamine supersensitivity. In a 6-week double-blind trial of tryptophan-benserazide we studied the relationship between tardive dyskinesia and psychotic relapse in 32 patients with process schizophrenia (5). Half of the subjects received tryptophan-benserazide instead of their regular neuroleptic medication and half received chlorpromazine. In the tryptophan group, the severity of tardive dyskinesia (assessed on a 9-point clinical impression scale of the Extrapyramidal Symptom Rating Scale [2]) tended to be greater in the 8 patients who deteriorated than in the 6 patients who did not (means±SD=5.4±1.4 and 3.8±1.7, respectively, $t=1.85$, $p<.10$). However, there was no difference in severity of tardive dyskinesia between the deteriorated (N=2) and nondeteriorated (N=14) chlorpromazine patients (means±SD=3.5±0.7 and

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3.9±1.9, respectively) or between the nondeteriorated patients in the two drug groups.

These results are consistent with the hypothesis that the relationship between severity of tardive dyskinesia and psychotic decompensation may be due to a common underlying mechanism of increased dopaminergic function covertly induced by long-term use of neuroleptics and made overt by drug discontinuation. There was no evidence that increased agitation caused a worsening of tardive dyskinesia, since the 2 deteriorated chlorpromazine patients did not show signs of having more severe tardive dyskinesia than the nondeteriorated tryptophan-benserazide patients.

Psychosis associated with sudden decline in prolactin levels. In a pilot study designed to test whether penicillin has an antipsychotic effect, 10 hospitalized schizophrenic patients chronically treated with neuroleptics had their medication withdrawn and replaced with oral penicillin for 6 weeks (6). Greater decreases in prolactin (geometric mean=22.6 ng/ml, range=11.7–51.7 ng/ml on day 0; geometric mean=6.0 ng/ml, range=3.7–10.3 ng/ml on day 42) tended to be associated ($r=.62$, $df=6$, $p<.10$) with symptomatic deterioration (mean BPRS total scores ±SD=37.5±8.8 on day 0 and 46.1±13.2 on day 42), and increased severity of tardive dyskinesia was significantly correlated with decreases in prolactin ($r=0.85$, $df=6$, $p<.01$).

There is evidence to suggest that supersensitivity does not occur in response to chronic dopamine blockade in the dopamine hypothalamoinfundibulum tract (7), so the extent of prolactin elevation can be seen as a measure of absolute dopamine blocking. That some patients require more dopamine blocking to control their symptoms, as suggested by their elevated prolactin levels, and relapse suddenly when the dopamine blocking is removed is consistent with the hypothesis that these patients have developed a supersensitivity in their mesolimbic dopamine receptor sites as they have in the neostriatum.

Discussion

The association between dyskinesia and psychotic relapse has been observed by others (8, 9). The hypothesis that tardive dyskinesia and supersensitivity psychosis may be caused by a similar mechanism occurring in different areas of the brain is suggested by the common factors that can alter the clinical picture of both syndromes: increasing the neuroleptic dosage decreases the severity of dyskinesia and psychosis, decreasing the dosage makes both worse, stress exacerbates both dyskinetic and psychotic symptoms, and L-dopa and amphetamine can increase the severity of both.

We suggest that neuroleptics can produce a dopamine supersensitivity that leads to both dyskinetic and psychotic symptoms. An implication is that the tendency toward psychotic relapse in a patient who has developed such a supersensitivity is determined by more than just the normal course of the illness. This may explain why Hogarty and associates (10) were unable to identify "good prognosis" patients who do not relapse when maintenance neuroleptics are discontinued.

Another implication is the possibility that this supersensitivity is irreversible. This is accepted to be true of tardive dyskinesia unless it is diagnosed early and medication is discontinued. If the same irreversibility is occurring in the mesolimbic region, the result would be patients who must remain on neuroleptics for the rest of their life regardless of the natural course of their illness. In the studies done by Hogarty's group, two-thirds of patients thought to be suitable for drug withdrawal after 2 years of drug therapy relapsed following drug discontinuation, causing the authors to state that "the need for maintenance chemotherapy may be indefinite" (10). In some of these cases, the need for continued neuroleptic treatment may itself be drug-induced.

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