

Reversing drug-induced parkinsonism

AGITATION, anxiety, depression—it's a common triad in elderly patients and a common solution is drug treatment with one of the potent phenothiazines or butyrophenones. But in some cases, drug treatment means exchanging troublesome mental symptoms for the equally troublesome physical symptoms of tremor, rigidity, and bradykinesia—a syndrome known as drug-induced parkinsonism.

It can occur in patients of any age but the elderly are particularly susceptible, says Dr. Ali H. Rajput, professor of neurology at the University of Saskatchewan in Saskatoon, Canada. Decreased levels of homovanillic acid and dopamine in the striata and substantia nigra—the hallmark of idiopathic paralysis agitans—may predispose some patients to parkinsonism when they are given dopamine antagonists. Indeed, these biochemical abnormalities were evident on autopsy in two older psychiatric patients who were placed on neuroleptic drugs and subsequently had a Parkinson-like reaction, Dr. Rajput and Drs. Bohdan Rozdilsky, Oleh Hornykiewicz, Tyrone Lee, and Phillip Seeman and Kathleen Shannak report in *Archives of Neurology* (vol. 39, p. 644). Although the symptoms gradually disappeared in both pa-

tients after the neuroleptics were withdrawn—and before each died of unrelated causes—the investigators believe they've hit upon the mechanism behind drug-induced parkinsonism: borderline dopamine deficiency so mild that symptoms remain quiescent until provoked.

"The degree of borderline parkinsonian changes and dopamine deficiency may determine how easily drug-induced parkinsonism develops in a given patient," Dr. Rajput explains, "but until the patient shows clinical manifestations of parkinsonism, there's no way of knowing he has those changes in the brain."

The potential for trouble certainly looms large. According to Dr. Rajput, about 1% of people over age 60 have Parkinson's disease, with the incidence rising to about 2.5% at age 80. Parkinsonian symptoms in these patients almost certainly worsen during phenothiazine treatment, he finds. Indeed, the incidence of parkinsonian symptoms could increase to 5% or even higher in all older patients given phenothiazine treatment, he estimates—which might explain why drug-induced parkinsonism is now the second commonest form of the disease.

The more potent the anti-psychotic agent, the more

likely it is to produce parkinsonism. If drug treatment is continued for long periods, tardive dyskinesias—the choreiform movements of the face, trunk, and extremities that resemble Huntington's chorea—will also develop.

Fortunately, drug-induced parkinsonian symptoms are usually reversible. When the medication is withdrawn, symptoms gradually disappear. In some patients with serious psychiatric symptoms, however, the medication can't be withdrawn. "In that case, you are committed to putting them on anti-parkinsonism medication," says Dr. Rajput. "The best choice for these patients is usually an anticholinergic drug."

It's a common practice in psychiatry to prescribe anticholinergics for any elderly patient taking a potent psychotherapeutic drug but Dr. Rajput advises against it. "Anticholinergics have their own side effects," he notes, "specifically urinary retention, constipation, and confusion, and there are indications that their prophylactic use may make a patient more prone to tardive dyskinesia. Rather than give medication in the expectation that parkinsonism is eventually going to develop, it's best to wait and see if symptoms occur." □