It is suggested that those who bear the responsibility for giving neuroleptics to elderly individuals be strongly advised not to exceed the prescribed doses and to inform the physician immediately if rigidity, confusion, and fever should develop. It is notable that this risk factor of rapid dose escalation was apparently avoided in most of the 10 elderly subjects in Pearlman's review.[4] Their susceptibility could be more related to age-related decreases in striatal dopaminergic reserve.[10]

Fever may be an unreliable sign of NMS in the very elderly population, because the capacity to develop a febrile response is often limited in this age group. This deficiency was illustrated in our case, where even the subsequent development of a pneumonia led only to a modest temperature elevation.

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Marijuana and Tourette's Syndrome

Editors:

Although a variety of pharmacological agents have been reported to attenuate symptoms of Tourette's syndrome (TS), the pathophysiology of this disorder remains unknown. Apart from the presence of disabling motor and vocal tics, TS patients often experience behavioral disturbances including obsessive compulsive thoughts, anxiety, depression, abnormal sexual behavior, attention deficit, learning disabilities, and sleep disturbances.[1] Drug abuse to obtain relief from the chronic anxiety may be common among these patients.[2, 3] We recently encountered three patients with TS who experienced incomplete responses to conventional anti-TS drugs but noted a significant amelioration of symptoms when smoking marijuana.

The first patient was a 15-year-old boy who, in addition to motor tics, had obsessive compulsive and self-mutilatory behavior. Treatment with haloperidol and clonidine were ineffective, but his obsessive thoughts and self-mutilatory behavior improved with administration of imipramine (37.5 mg/day) combined with the oral opiate receptor antagonist naltrexone (dose range 50 to 100 mg/day). During recreational use of marijuana (1 to 2 cigarettes/day), he noted general relaxation and marked lessening in his urge to tic. According to the patient's mother, motor tics had decreased by about 50% and there was also some reduction in the frequency of the self-mutilatory behavior. The patient had been smoking marijuana for 4 weeks, and upon discontinuation, noted rebound exacerbation of symptoms within 12 hours.

The second patient, age 17, had had severe motor tics since the age of 7 years. He had frequent jerk-type movements of his neck muscles associated with infrequent vocalizations during stressful situations. His management had been difficult as he was unable to tolerate haloperidol or clonidine. Administration of naltrexone (150 mg/day) reduced his anxiety level and the urge to tic; this was the only drug he could tolerate. On several occasions, he had smoked marijuana and noted generalized relaxation accompanied by reduction in the severity of the motor tics and improvement in attention span. He volunteered that smoking one cigarette reduced the frequency of his motor tics by about 60% to 70%, which was sustained over several hours.

The third patient was a 39-year-old man who had had symptoms of TS since the age of 9 years. His symptoms included frequent jerking-type movements of his neck and upper extremity muscles, facial grimacing, frequent blinking, and leg jerking. Vocalizations were not noted except during extreme anxiety. In addition he was troubled by chronic insomnia and hypersexuality. He reported no benefit from haloperidol, clonidine, or benzodiazepines but experienced some relief after consuming large amounts of ethanol. He also admitted that marijuana smoking (½ to 1 cigarette/day) produced relaxation with subsequent reduction in the severity of the motor tics along with marked attenuation of his hypersexuality.

From 1842 to the turn of this century, several reports in the literature have indicated that marijuana smoking was used extensively as an analgesic, sedative, and hypnotic agent.[4] Moreover, oral cannabis preparations were useful in the management of diverse neurological conditions including convulsions and chorea.[5] Much more recently it was reported anecdotally that patients with dystonia improved with their alleged cannabis smoking.[6] The cannabis constituent cannabidiol was reported efficacious in reducing symptoms of dystonia[7, 8] and Huntington's chorea.[9] In experimental animals, cannabidiol has been shown to exert anticonvulsant and antianxiety properties and affect apomorphine-induced turning behavior in rats.[10] The latter report suggested that cannabidiol exerts antidyskinetic effects through modulation of striatal dopaminergic activity. Tetrahydrocannabidiol (THC, the active compound of marijuana) may exert GABA-ergic as well as antiserotonergic effects.[11] A recent report has demon-

strated that THC reduces opiate receptor binding sites and modulates μ and δ opioid receptors in a noncompetitive manner.[12] THC may also exert effects on the cholinergic system.[13]

Considering evidence that marijuana may exert effects on a large number of neurotransmitters, it is difficult to speculate on its mode of action in attenuating symptoms of TS. It is reasonable to assume that the effects of marijuana in TS may be largely related to its anxiety-reducing properties, although a more specific antidyskinetic effect cannot be excluded. Should marijuana compounds prove to have specific actions in TS, chemical modifications which eliminate the psychoactive properties while retaining the antidyskinetic effects (e.g., cannabidiol) could promise a new class of drugs useful in the management of TS. Further studies are clearly needed in both the clinical and basic laboratory realms to further characterize the effects of cannabinoids in TS.

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Lithium-Induced Akathisia*

Editors:

Extrapyramidal side effects associated with lithium maintenance therapy have been widely reviewed.[1–5] To date, only one case report of lithium-induced akathisia is presented in the literature.[6] In that instance, the akathisia was dose dependent. I report here a case of lithium-induced akathisia that was not dose dependent and was resistant to amelioration by anticholinergic agents.

A 54-year-old man was admitted to the hospital following several weeks of manic behavior during which he frivolously spent large sums of money. He responded to haloperidol in a dosage of 20 mg/day. Lithium carbonate was begun concurrently at 900 mg/day. Physical examination and a complete laboratory evaluation including a CBC, SMAC-20, urinalysis, thyroxine, thyroid-stimulating hormone, EEG, and CT scan did not reveal an etiology for his mania.

Shortly after lithium therapy was begun, the patient felt intense restlessness in his legs. He experienced a compulsive need to move about the ward. Haloperidol was discontinued, but the akathisia persisted. No response was obtained with amantadine or trihexyphenidyl. A week following discontinuation of haloperidol, the lithium carbonate was discontinued and the akathisia cleared within 24 hours. The patient did well and was discharged to outpatient follow-up.

One month after discharge, with the informed consent of the patient, lithium carbonate was restarted at a dosage of 900 mg/day. The patient developed akathisia within 24 hours, and the therapy was discontinued because of the intolerable akathisia. Frequent follow-up was substituted for prophylactic therapy.

Speculation as to the mechanism of action involved in this case is not possible at this time. It does appear that akathisia can, albeit rarely, be a prohibitive side effect to lithium maintenance therapy.

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