

malization after longer-term treatment (1 year) has been reported (6).

It may be advantageous to avoid the use of directly acting dopaminergic agents in psychotic patients because of the risk for worsening psychosis. Whether this risk is really any lower for aripiprazole when combined with a direct D₂ receptor antagonist is not clear and would need to be answered in a controlled trial.

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Clozapine-Induced Allergic Vasculitis

TO THE EDITOR: Recently, a patient in our institution developed palpable purpura shortly after initiation of the antipsychotic clozapine. Palpable purpura is an indication of inflammatory hemorrhage and is highly suggestive of allergic vasculitis. A literature search revealed no prior reported cases. We are reporting this case of clozapine-induced allergic vasculitis to promote a swifter diagnosis and treatment of this rare complication.

Mr. A was a 59-year-old man with a history of paranoid schizophrenia, deafness, hypothyroidism, and tardive dyskinesia. Haloperidol was being discontinued and clozapine initiated because of persistent extrapyramidal symptoms, tardive dyskinesia, and treatment-resistant psychotic symptoms. Clozapine had been introduced 17 days earlier and was being slowly titrated upward. Besides haloperidol, his other medications included benztropine, divalproex sodium, lorazepam, trazodone, and levodopa. When the total dose of clozapine was 137.5 mg/day, a rash developed on his legs. The rash was a confluent, nonblanching, erythematous, elevated patch consistent with a palpable purpura. It continued to spread up his lower extremities but never involved his palms or soles. He was afebrile with stable vital signs and had a benign examination otherwise. Aside from the clozapine, treatment with all other medications was longer than 2

months, with haloperidol, benztropine, and divalproex sodium having been administered for more than 10 years.

The initial differential diagnosis included Rocky Mountain spotted fever, Churg-Strauss syndrome, Wegener's granulomatosis, microscopic polyarteritis, mixed cryoglobulinemia, and Henoch-Schönlein purpura. Mr. A was empirically administered doxycycline in case of Rocky Mountain spotted fever, and his divalproex sodium and clozapine doses were held steady. Rocky Mountain spotted fever was ruled out by serology and by the fact that Mr. A had been indoors (hospitalized) for the last 2 months. Churg-Strauss syndrome was unlikely because he did not have a history of asthma or eosinophilia. The results of urine and blood cultures and serologies (CBC, liver function tests, creatine kinase, erythrocyte sedimentation rate) were all unremarkable. He was transferred to a tertiary care center for further evaluation. Mr. A was managed conservatively without steroids and had further serologies (serum cryoglobulins, complement C3, complement C4, hepatitis C, and antineutrophil cytoplasmic antibodies studies) whose results were negative. A punch biopsy of his skin revealed perivascular neutrophilic infiltrate with extravasation of red blood cells, suggestive of early leukocytoclastic vasculitis.

The diagnosis of allergic vasculitis was made because of Mr. A's age, recent medication adjustments, and the isolated skin involvement (1). A closer review of his medications revealed that clozapine was the only new medication in the last 2 months. He improved with conservative management, and it was decided not to rechallenge him with clozapine.

Clozapine is the drug of choice for schizophrenia patients with persistent residual symptoms. Clozapine-induced allergic vasculitis is a rare but serious complication that should be added to the adverse reactions to clozapine therapy. We hope that this case will promote awareness and expedite diagnosis and treatment of this adverse reaction.

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Smokeless Tobacco for a Nicotine-Dependent Schizoaffective Patient

TO THE EDITOR: Approximately 83% of the patients with schizophrenia and 65% with mood disorders are nicotine dependent (1). The following case demonstrates the benefit of switching from smoking to oral tobacco in a severely nicotine-dependent psychiatric patient.

Ms. A, a 52-year-old woman with schizoaffective disorder, bipolar type, started smoking shortly after her first psychotic episode at age 19 and, on average, smoked about 1½ packs per day for 33 years. She had attempted to quit using pharmacotherapy, nicotine gum, or patches in combination with cessation classes. Both gum and patch treatments were ineffective since they did not control her craving for cigarettes. Her motivation to quit was strong because of the sequelae of smoking: bronchitis,

isolation from others, and destabilization of her psychiatric illness from frequently awakening to smoke. Her brother with a bipolar disorder had experienced severe burns over most of his body and died secondary to a fire caused by his smoking. For her, smoking had become a constant reminder of his suffering, which led to nightmares and further isolation. She was afraid to jeopardize the health and safety of others.

One year ago, she was cross-titrated over a 1-week period to oral pouches. Since that time, she has not resumed smoking, and her psychiatric and medical symptoms have stabilized. Before her cessation of smoking, she lived an isolated existence. Now she resides with and cares for her parents. For Ms. A, ceasing to smoke was a life-changing event.

Using smokeless tobacco is less deleterious to health and less socially stigmatizing than cigarette smoking. According to Dr. Rodu, dentist and oral pathologist, switching to smokeless tobacco considerably reduces the risk of all cancers, including oral cancer. Rodu and Cole (2) published similar results in *Nature*, demonstrating that the life expectancy of a 35-year-old smokeless tobacco user is relatively the same as that of a nonuser, while a smoker's life expectancy is around 7.8 years less than both the nonuser's and the smokeless tobacco user's life expectancy. Because long-term success rates of nicotine-substitution products are often low, the substitution of smokeless tobacco may be more desirable for individuals who have failed traditional techniques of cessation. These results—along with population-based studies demonstrating decreased relative risks for cardiovascular, respiratory, and oncological disease with smokeless tobacco compared to smoking—have prompted a pilot study using smokeless tobacco as a substitute for smoking in inveterate smokers. This study found a 25% cessation of cigarette use at the 1-year mark (3). These data, combined with the experience of our patient, suggest that in select patients, smokeless tobacco may be less harmful than continued smoking.

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Comfort, Self-Confidence, Safety, and Dopamine D₂ Receptor Occupancy by Antipsychotics

TO THE EDITOR: Antipsychotics are thought to influence the subjective well-being of patients, depending on the occupancy of these receptors (1–3). Drug-induced dysphoria is related to quality of life and medication compliance. It may also be a sensitive marker for too high dopamine D₂ receptor occupancy caused by conventional and newer-generation an-

tipsychotics (1–3). However, adverse mental effects of antipsychotics are difficult to differentiate from primarily negative symptoms and depressive symptoms, and little is known about which aspects of subjective experience are most strongly related to D₂ receptor occupancy.

We sought to identify which aspects of subjective well-being are most strongly related to D₂ receptor occupancy by conventional and newer-generation antipsychotics.

An analysis was performed on the combined data of two previous studies (2, 3). These studies were approved by the ethics committee of the Academic Medical Centre, Amsterdam, the Netherlands. The subjects, 50 patients, 48 with recent-onset schizophrenia and two with schizoaffective disorder, were diagnosed according to DSM-IV criteria; 45 were men, and the mean age was 22.1 years (SD=2.5).

The patients' subjective experience was measured with the Subjective Well-Being Under Neuroleptics Scale (4) after a stable dosing period of at least 6 weeks of olanzapine (N=27, mean=11.2 mg/day, SD=4.5), risperidone (N=12, mean=3.6 mg/day, SD=1.1), or haloperidol (N=11, 2.5 mg/day). Higher scores on the Subjective Well-Being Under Neuroleptics Scale imply more favorable subjective well-being. To determine the levels of striatal D₂ receptor occupancy, [¹²³I]IBZM single photon emission computed tomography imaging was performed. Specifications of comparison group, imaging procedures, and data analyses have been described elsewhere (1, 2).

All 38 items from the Subjective Well-Being Under Neuroleptics Scale were negatively correlated with D₂ receptor occupancy, with 28 items reaching statistical significance (Spearman's correlation, two-tailed). The highest correlations were found for five items on the Subjective Well-Being Under Neuroleptics Scale that could be described as "feeling comfortable, self-confident, and safe": "I feel very comfortable with my body" ($r_s=-0.448$, $df=49$, $p=0.001$), "My body is a burden to me" ($r_s=-0.433$, $df=49$, $p=0.002$), "I am full of confidence, everything will be all right" ($r_s=-0.429$, $df=49$, $p=0.002$), "I do what I want to do and know how to assert myself" ($r_s=-0.419$, $df=49$, $p=0.002$), and "I feel safe and secure" ($r_s=-0.382$, $df=49$, $p=0.006$).

Negative subjective experiences are related to D₂ receptor occupancy by conventional and newer generation antipsychotics. Monitoring feelings of comfort, self-confidence, and safety may guide clinicians and researchers to find optimal D₂ receptor occupancy. To test this hypothesis, however, more research is needed.

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