To submit questions for this regular feature, please send them to the Journal of Psychiatry & Neuroscience / Revue de psychiatrie & de neuroscience, *Canadian Medical Association, 1867 Alta Vista Dr., Ottawa ON K1G 3Y6, Canada; fax 613 729-9545; jpn.office@sympatico.ca. Please include details of any relevant case and your name, address, telephone and fax numbers as well as your email address.*

What is the role of pharmacotherapy in tobacco cessation in patients with schizophrenia?

Tobacco use is the leading preventable cause of death and disease in our society, and the prevalence of smoking in individuals with schizophrenia is significantly higher than in the general population (up to 88% v. 20%). Additionally, the risk of cancer in individuals with schizophrenia is increased. In patients with weight gain and diabetes associated with atypical antipsychotic drug use, the risk of cardiovascular death may be further increased.

Forced abstinence from nicotine is associated with significant adverse outcomes and is contraindicated in this population. Nicotine replacement therapy (NRT) should be routinely offered to individuals who wish to quit smoking. NRT appears to be both safe and indeed imperative for successful outcomes in tobacco cessation treatment of patients with schizophrenia. The combination of nicotine transdermal patches and nicotine polacrilex gum is advised. Although patients are generally discouraged from smoking while using NRT, cautiously allowing this practice appears to keep them engaged in the process, and the dangers may be overrated. Care should, however, be exercised in the dosing protocol of NRT, assuring adequate nicotinic receptor saturation, with the possibility of cautiously exceeding labelled indications (dose *and* duration) for heavy smokers.

Bupropion is thought to be safe and effective in individuals with schizophrenia and, with adequate blood pressure monitoring, could be combined with NRT. Higher doses of bupropion should be used with caution because of the quite frequent existence of a genetic polymorphism for cytochrome P450 2B6 (CYP2B6). Slow metabolizers of bupropion may have high circulating blood levels, further lowering the seizure threshold when combined with clozapine, necessitating adequate seizure prophylaxis (e.g., divalproex sodium).

The use of clozapine (to ameliorate mesolimbic dopaminergic dysregulation) has been associated with a reduction in smoking, whereas the use of typical antipsychotics has been associated with increases in smoking behaviour. The combined use of NRT and atypical antipsychotics appears to be superior to typical antipsychotics combined with NRT in smoking cessation trials in combination with psychosocial interventions. Polynuclear aromatic hydrocarbons in cigarette smoke induce cytochrome P450 1A2 (CYP1A2), which is partially responsible for the metabolism of clozapine, olanzapine and quetiapine. Smoking cessation may interfere with metabolism in that CYP1A2 induction may be reversed, leading to increased bioavailability and higher (and even toxic) plasma levels of clozapine and olanzapine. Neither nicotine (metabolized by CYP2A6) nor bupropion (metabolized by CYP2B6) is expected to alter the pharmacokinetics of each other or of the atypical antipsychotics.

Individuals with schizophrenia and tobacco dependence should be offered intensive multimodal treatment, including NRT at adequate doses of optimal duration and, in selected individuals, bupropion. Caution should be exercised to avoid the development of toxic levels of olanzapine or clozapine in patients who quit smoking or manage to reduce their consumption (below 10 cigarettes/d). Pharmacologic and nonpharmacologic interventions, including advocacy for a smoke-free environment, should form part of an intensive multimodal treatment plan, with special attention to compliance.

Charl Els, MB ChB, MMed (Psych)
Department of Psychiatry
University of Alberta
Edmonton, Alta.

Competing interests: Dr. Els has conducted continuing medical education for Janssen-Ortho, Eli Lilly, AstraZeneca, Wyeth and GlaxoSmithKline.

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided.