Psychopharmacology for the Clinician
Psychopharmacologie pratique

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.

Psychopharmacology of smoking cessation in patients with mental illness

A 48-year-old male smoker (35 cigarettes a day for 30 years) with major depressive disorder stabilized on citalopram, 40 mg once daily, wished to quit smoking. Whenever he quit "cold turkey," he relapsed owing to intolerable anxiety and depression that twice met criteria for an acute depressive episode. His psychiatrist added bupropion SR, 150 mg twice daily. He was advised to quit within 2 weeks. His anxiety increased within a few days of quitting but resolved with a reduction in caffeine consumption. He discontinued bupropion after 12 months. He gained 1 kg, remained euthymic and had occasional mild cravings with minimal anxiety.

Tobacco causes almost 48 000 premature deaths in Canada annually (Makomaski and Kaiserman, *Can J Public Health* 2004;95:38-44). Those with past-month psychiatric diagnoses consume 44% of all cigarettes (Lasser et al, *JAMA* 2000;284:2606-10). This significant association is due to a combination of genetic (e.g., P50 deficits in schizophrenia corrected by nicotine), environmental (e.g., pro-smoking policies in patient group homes) and other factors (e.g., "self-medicating behaviours" to reduce anxiety and depression; the use of cigarettes as rewards to shape behaviour). The adverse effects are amplified by obesity and metabolic changes owing to psychotropic drugs and poverty. Fortunately, there is a 50% risk reduction in coronary events within 1 year of quitting and a significant reduction in the risk of developing lung disease and cancer in the long-term.

Bupropion has a large effect size in permanent smoking cessation (19 trials, odds ratio 2.06, 95% confidence interval 1.77–2.40) independent of its antidepressant effects (Hughes et al, *Cochrane Database Syst Rev* 2004; [4]:CD000031), with 15% quitting permanently with minimal weight gain. It is also effective in smokers with depression and schizophrenia (Dudas and George, *Essent Psychopharmacol* 2005;6:158-72). Bupropion may stabilize the dopaminergic reward system and competitively antagonize nicotine at central $\alpha 4\beta 2$ nicotinic receptors (Warner and Shoaib, *Addict Biol* 2005;10:219-31). Clinically, subjects report decreased cravings and cigarette taste aversion. Responders tend to be moderately dependent male smokers who have tried to quit previously (Hurt et al, *Addict Behav* 2002;27:493-507). Smokers with the low activity variant (CT/TT group) of CYP2B6 are less likely to be abstinent than are smokers with normal activity variants (CC group) ($\chi^2 = 5.0$, $p < 0.02$) (Munafo et al, *Pharmacogenomics* 2005; 6:211-23). Bupropion is safe in combination with most neurotropic drugs because it is primarily metabolized by CYP 2B6. However, dose reduction in concomitant caffeine, benzodiazepines and neuroleptic drugs (especially clozapine) may be warranted, because polyaromatic hydrocarbons present in smoke induce CYP 1A2. The induction reverses within days to weeks after smoking cessation.

Doses of 150 mg or 300 mg are effective within 3 weeks, but there are no studies with higher doses. Motivated smokers may also respond after 4 weeks of therapy. Thereafter, nicotine replacement therapy may be added. Relapse is common on stopping the medication, even after a year, necessitating longer-term use in some smokers (Hays et al, *Ann Intern Med* 2001; 135:423-33).

Insomnia can be minimized by timing the second dose to be no later than 6 hours before bed. Seizures (1/2000) can be prevented by not exceeding the recommended dose and by observing contraindications.

In conclusion, psychiatrists have the ability to treat smokers in their practice with a common psychiatric medication with good efficacy.

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Psychopharmacology for the Clinician columns are usually based on a case report that illustrates a point of interest in clinical psychopharmacology. They are about 500 words long, and references are not necessary.
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