Discontinuing treatment for psychiatric disorders

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The psychopharmacology of major psychiatric disorders involves the principle of optimal treatment, which includes appropriate drug selection, correct dosing, recognition and management of side effects, and appropriate duration of treatment. There is a substantial literature to support evidence-based decisions for all of these components of treatment in most major psychiatric syndromes. Less attention has been focused on drug discontinuation, especially in an era when longer-term treatment is recommended for most mood, anxiety and psychotic disorders. However, the rate and method of drug discontinuation can affect the course and prognosis of both mood and psychotic disorders. This is particularly relevant given the recommended use of relatively brief antidepressant treatment in bipolar disorder and the intermittent use of antipsychotic drugs in both mood and psychotic disorders. Moreover, up to 50% of patients will not comply with their prescription medication and will discontinue their drug treatments of their own accord.[1]

Analogous observations have been made in bipolar disorder and schizophrenia concerning drug discontinuation. Several studies have shown that discontinuation of lithium maintenance treatment in patients with bipolar disorder whose condition has been stabilized leads to a significantly higher and earlier risk of recurrence, particularly for mania.[2,3] Moreover, rapid versus gradual discontinuation of lithium leads to a substantially higher risk of recurrence, especially in the first few months of follow-up.[3] In schizophrenia, discontinuation of oral neuroleptic drugs also increases the risk of recurrence, especially within the first 6 months after cessation of treatment.[4] It would, therefore, seem that discontinuation either due to patient noncompliance or as a therapeutic intervention because of lack of effectiveness or in order to substitute an alternative treatment may profoundly affect the course and outcome of these major psychiatric disorders. There are comparable data to support an increased risk of recurrence with discontinuation of antidepressants in both unipolar depression[5] and anxiety disorders.[6] These observations across psychiatric syndromes have potentially powerful implications. First, stopping and starting various drugs, regardless of their therapeutic benefit, may alter the course of the illness being treated. Substitution of an antidepressant, antipsychotic or mood stabilizer may, in effect, amount to discontinuing the first treatment. Although there is no reason to avoid such clinical interventions, careful observation and systematic study may be warranted to document any potential adverse discontinuation effects during therapeutic substitution, especially if the first medication is rapidly discontinued. Second, patient noncompliance may not only cause short-term difficulties but, if it occurs abruptly, may alter the longer-term prognosis of their illness. Patients may need more education about the adverse impact of discontinuation, especially when abrupt, on the prognosis of their disorder. Last, systematic study is required to quantitate the potential adverse impact of medication changes and medication substitution as part of the normal therapeutic process on the outcome of the disorder. There is accumulating preclinical evidence of functional and neurobiological changes with antidepressant discontinuation that may be the biochemical analogues of the above-mentioned clinical observations.[7]

Discontinuation of medications presents additional problems. Discontinuation of all antidepressants, particularly the selective serotonin reuptake inhibitors, with the possible exception of fluoxetine, is associated with a discontinuation syndrome that presents with flu-like and gastrointestinal symptoms, which can be ameliorated with a gradual tapering or reintroduction of the antidepressant.[8] Sudden antidepressant withdrawal may also provoke mania or hypomania in some patients regardless of whether previous spontaneous manias have occurred.[9]

In the Psychopharmacology for the Clinician column in this issue (page 72),[10] Serge Gauthier extends some of these observations to patients with dementia and the use of

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donepezil. His observations and caution underscore the importance of drug discontinuation as an important factor in the management and course of all major psychiatric disorders. Not only may there be short-term ill effects for the patient but there may also be a risk of long-term adverse consequences for the patient's illness.

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JPN's Top Ten Articles, December 2005
(based on Web views on PubMed Central)

1. **Perinatal complications in children with attention-deficit hyperactivity disorder and their unaffected siblings**
   Ben Amor et al
   J Psychiatry Neurosci 2005;30(2):120-6
2. **Potential benefits of quetiapine in the treatment of substance dependence disorders**
   Sattar et al
   J Psychiatry Neurosci 2004;29(6):452-7
3. **Substance use and cognition in early psychosis**
   Pencer and Addington
   J Psychiatry Neurosci 2003;28(1):48-54
4. **Treatment of primary insomnia with melatonin: a double-blind, placebo-controlled, crossover study**
   Almeida Montes et al
   J Psychiatry Neurosci 2003;28(3):191-6
5. **Effects of diazepam on facial emotion recognition**
   Coupland et al
   J Psychiatry Neurosci 2003;28(6):452-63
6. **Use of the Medication Event Monitoring System to estimate medication compliance in patients with schizophrenia**
   Diaz et al
   J Psychiatry Neurosci 2001;26(4):325-9
7. **Antidepressant-like activity of S 20098 (agomelatine) in the forced swimming test in rodents: involvement of melatonin and serotonin receptors**
   Bourin et al
   J Psychiatry Neurosci 2004;29(2):126-33
8. **Genetic and neurobiological aspects of attention deficit hyperactive disorder: a review**
   Hechtman
   J Psychiatry Neurosci 1994;19(3):193-201
9. **Information-processing deficits and cognitive dysfunction in panic disorder**
   Ludewig et al
   J Psychiatry Neurosci 2005;30(1):37-43
10. **Heroin and cocaine co-use in a group of injection drug users in Montréal**
    Leri et al
    J Psychiatry Neurosci 2004;29(1):40-7