

## Substance Abuse and Schizophrenia

Substance *abuse*, i.e., recurrent substance use leading to occupational or social impairment, etc., may have different implications from substance *dependence*, i.e., tolerance, withdrawal, frequent or high dose abuse, etc. (see DSM-IV) Patients who intermittently abuse substances may generally be treated with the basic algorithm. Patients who are actively substance dependent need treatment provided for their substance abuse as well as their schizophrenia with the courses of treatment administered simultaneously. Substance abusing schizophrenic patients are 8-13 times more likely to be noncompliant<sup>1</sup> and show poor results even when their medication is actually taken.

If the patient is actively dependent upon substances, detoxification is advised as part of the initial treatment of the psychosis. At least some of the patient's symptoms may be due to the direct physiological effects of the substance, and these may improve after detoxification. Non-specific behavioral tranquilization may be necessary during this process, often with the same medications used to treat the primary psychotic disorder. but this must be done with care so as to avoid toxic interactions with the particular substance(s) of abuse that are on board. For example, prescribed benzodiazepines are ideally avoided,<sup>2</sup> except as part of alcohol and sedative detoxification.

A "Dual-Diagnosis" treatment approach is usually advised as the next step for these patients. Relapse-prevention counseling, 12 step programs, and/or cognitive-behavioral interventions are recommended. Patients may need structured living situations that emphasize abstinence and contain the necessary supervision, while accepting the patients' need for antipsychotic medication for their schizophrenia. Despite prevalence estimates ranging from 40 to 75%, screening and treatment for this problem is frequently not occurring in public care systems, and this fact may account for some of the poor outcome and treatment-resistance of these patients.

Systems of care that integrate substance abuse rehabilitation and recovery with mental illness treatment and rehabilitation appear to be the ideal.<sup>3</sup> After acute stabilization, patients should be engaged in an ongoing education process for both disorders, and there should be clear-cut policies on responses to problematic behaviors.<sup>3</sup>

### The impact of substance abuse on the treatment of schizophrenia

Co-morbid substance abuse is common, often undetected, and adversely affects outcomes in patients with schizophrenia. In the Epidemiologic Catchment Area Study sample of patients in community and institutional settings in the US, 47% of schizophrenia subjects met criteria of substance abuse or dependence (1).<sup>4</sup> Alcohol, followed by cocaine and cannabis, was the drug most frequently reported by schizophrenia patients (1)<sup>4</sup>, although

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<sup>1</sup> Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophrenia Bull* 1997;23(4):637-651.

rates of amphetamine use have been very high in some studies relying on laboratory measures rather than self-report 5(2). Nicotine is not included among abused substances in these estimates of prevalence. Substance abuse patterns in patients with schizophrenia appear to reflect community patterns rather than underlying symptom profiles or other clinical factors 6(3). Studies employing analysis of urine and hair samples have demonstrated that self-reports of substance abuse in schizophrenia patients are highly unreliable, as are physician assessments of substance abuse or intoxication (2, 4). 5, 8 Comorbid substance abuse has been associated with refractory psychotic symptoms, anxiety, depression, poor treatment compliance, relapse, violence, suicide, tardive dyskinesia, and infection with hepatitis and human immunodeficiency virus (HIV) (3, 5-7).

### **Patient Assessment:**

The presence of substance abuse should always be explored as part of the assessment of patients with schizophrenia. Because self-reports are often unreliable, additional source of information should be utilized, including past records, other informants, and laboratory analysis of urine, blood or hair samples. Factors that may suggest substance abuse include persistent psychotic symptoms, frequent relapse, violence, or treatment noncompliance. As part of this assessment, patients should also be tested for alcohol-related elevation of hepatic enzymes and serologic indices of HIV and hepatitis C infection.

### **Relevance of Substance Abuse to Pharmacologic Management:**

Careful assessment of covert substance abuse should be performed before altering pharmacologic treatment in response to inadequate response or relapse. Patients with substance abuse should be offered specialized treatment including motivational interviewing, cognitive behavioral therapy and family intervention (8). While many or most patients may not desire to stop substance use, treatment can be guided by their level of motivation (9). In cases in which comorbid substance use interferes with antipsychotic compliance, a depot antipsychotic should be considered. Preliminary evidence has suggested that clozapine treatment is associated with a spontaneous reduction in substance use and so may facilitate interventions aimed at comorbid substance abuse (10, 11). In addition, schizophrenia patients who are abusing substances have been found to respond to clozapine similarly to non-abusing patients. The relative potential benefit of other atypical agents for substance abusing patients, although advocated by some experts, remains to be established (12-15). While all antipsychotics attenuate behavioral effects of stimulants in animal models, clozapine appears to uniquely attenuate the psychotic exacerbation produced by NMDA receptor antagonists (ketamine or phencyclidine) in schizophrenia patients (16). A role for adjunctive agents, such as naltrexone and disulfiram has not been supported in schizophrenia patients, whereas some preliminary evidence supports the use of antidepressants in dysphoric substance abusing patients (17, 18).

Potential interactions between substances of abuse and antipsychotic medications must also be considered. Cigarette smoking substantially increases hepatic metabolism of many antipsychotic agents; for example, smoking cessation can result in large increases in serum clozapine concentrations (19). While clozapine can attenuate the euphoric and pressor effects of cocaine, it may also increase cocaine blood levels and may place patients at risk for syncopal episodes (20). In contrast, chronic haloperidol administration has been reported to decrease the dose of cocaine required to produce a euphoric response, presumably as a result of postsynaptic dopamine receptor upregulation (21).

(Goff and Osser)

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