## Managing Attention-Deficit/Hyperactivity Disorder in the Presence of Substance Use Disorder

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Patients with attention-deficit/hyperactivity disorder (ADHD), especially adolescents and young adults, commonly have comorbid conditions, including substance use disorder (SUD), which can complicate the treatment and management of both illnesses. Patients with ADHD and SUD have an earlier age at onset of SUD, may take longer to achieve remission than those with only SUD, and are likely to have a longer course, poorer outcome, and higher rates of other psychiatric comorbidities. There is evidence of misuse and diversion with stimulant medications, which raises several safety concerns. Studies of pharmacotherapy for ADHD and comorbid SUD are limited but have shown that stimulant medications probably do not exacerbate the SUD. Nonstimulant medications for ADHD and extended-release stimulant formulations are available and may be less likely to be misused or diverted. Understanding the motives for drug use and misuse is important in treating patients with ADHD and comorbid SUD. A number of tools are available to the clinician to detect substance use problems in patients with ADHD, including drug and alcohol screening questionnaires and toxicology screens. Clinical recommendations for treating this dual diagnosis include using nonstimulant agents or extended-release stimulant formulations in conjunction with psychosocial therapies to treat both the ADHD and the SUD. (J Clin Psychiatry 2007;68[suppl 11]:23-30)

A ttention-deficit/hyperactivity disorder (ADHD) is the most common emotional, cognitive, and behavioral disorder in children.<sup>1-3</sup> According to the American Academy of Pediatrics treatment guidelines,<sup>2</sup> ADHD affects an estimated 4% to 12% of school-aged children in the United States; a 2002 Mayo Clinic study found the prevalence to be 7.4%.<sup>3</sup> Those with ADHD have a high rate of comorbid psychiatric disorders, such as oppositional defiant disorder, conduct disorder, mood and anxiety disorders, and substance use disorder (SUD).<sup>4</sup>

One concern that parents and health care providers have is that treating ADHD with stimulants may lead to an increased risk for SUD as patients reach adolescence and adulthood. However, a meta-analysis<sup>5</sup> showed that the opposite may be true, that stimulant treatment of ADHD in childhood may lead to a reduced risk for subsequent SUD. A more recent study confirmed that finding.<sup>6</sup> Other evi-

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Corresponding author and reprints: Himanshu P. Upadhyaya, M.B.B.S., M.S., 67 President St., P.O. Box 250861, Charleston, SC 29425 (e-mail: upadhyah@musc.edu). dence also suggested that, besides preventing SUD in children with ADHD, treating adults with ADHD may also reduce the risk of SUD relapse.<sup>7</sup>

Another concern is the problem of drug diversion. Studies have shown that approximately a quarter of patients with ADHD are approached by others who want to buy stimulant medication<sup>8</sup> and that 11% have sold their medications.<sup>9</sup> In both of these studies,<sup>8,9</sup> ADHD patients with comorbid alcohol or drug use disorders were more likely to be involved in the illicit misuse or diversion of ADHD medications, and in 1 study,<sup>9</sup> those patients with comorbid conduct disorder were also more likely than those without to engage in these behaviors.

Managing comorbid ADHD and SUD requires a firm understanding of the *Diagnostic and Statistical Manual* of Mental Disorders, Fourth Edition, (DSM-IV)<sup>10</sup> criteria and the clinical presentations of the disorders. Differentiating among *abuse*, *misuse*, and *diversion* of prescription medications is also important, as is understanding patients' motives for abuse of their medications. No current guidelines or consensus statements exist for the management of ADHD and comorbid SUD, making treatment a special challenge for clinicians.

## OVERVIEW OF SUBSTANCE USE DISORDER AND ADHD

## **DSM-IV** Diagnostic Criteria

*Substance use disorder.* According to the DSM-IV,<sup>10</sup> the criteria for SUD include abuse, dependence, intoxication, and withdrawal. These criteria are applicable across

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all classes of substances, but abuse and dependence diagnoses are the most commonly used. For a diagnosis of abuse, a person must meet 1 or more of the following criteria in a 12-month period: have recurrent impairment as manifested by role impairment or inability to fulfill major obligations at home, work, or school; have recurrent legal problems related to substance use; repeatedly use substances in potentially hazardous situations such as driving or operating machinery; and have recurrent substance use despite related social or interpersonal problems. A diagnosis of substance dependence requires that, at any time within a 12-month period, a patient meet 3 of the following 7 criteria: tolerance; withdrawal; loss of control; attempting to quit or cut down; spending significant time obtaining, using, or recovering from the effects of a drug; impairment of regular activities; and psychological or physical problems caused or exacerbated by substance use.

Attention-deficit/hyperactivity disorder. For a diagnosis of ADHD, a patient has to meet 6 or more symptoms of inattention and/or hyperactivity/impulsivity for at least 6 months and to a degree that is disruptive and inappropriate for the patient's developmental level.<sup>10</sup> For example, parents may mistake toddlers' behavior to be an indication of hyperactivity, when it may in fact be normal behavior for that developmental phase. Additionally, the DSM-IV<sup>10</sup> requires that the impairing symptoms of hyperactivityimpulsivity or inattention present before 7 years of age and in 2 or more settings, such as school, work, home, and social settings. In clinical settings, it is important to identify this distinction. For example, the clinician may need to focus on helping parents improve their parenting skills rather than treating the child for ADHD if the impairment is solely at home. The final criterion for a diagnosis of ADHD includes symptoms that cannot be better accounted for by the presence of another disorder, such as a pervasive developmental disorder, psychotic disorder, or mood disorder.

#### Populations at Risk for Substance Use Disorder

The 2004 Substance Abuse and Mental Health Services Administration's National Survey on Drug Use and Health (NSDUH)<sup>11</sup> reported a prevalence rate for current (i.e., past month) illicit drug use of 3.8% for those aged 12 to 13 years, which steadily rose during the teen years to a high of 22.3% in those aged 18 to 20 years. The rate dropped with subsequent ages. The prevalence of SUD is equivalent in boys and girls aged 12 to 17 years. However, at 18 years and older, the prevalence of SUD is twice as high in men as in women. The data highlight the need for prevention and treatment efforts relating to SUD focused on adolescents and young adults.

#### **Commonly Abused Substances**

The Monitoring the Future survey,<sup>12</sup> which is sponsored by the National Institute on Drug Abuse, reported patterns





and trends of drug use in 8th, 10th, and 12th grade students, as well as college students and adults aged 19 to 45 years. In the sample of 8th, 10th, and 12th grade students, alcohol was the most frequently used substance in the past 30 days (Figure 1). Similar prevalence rates were reported among the 3 grade levels for tobacco use in the form of cigarettes, marijuana use, and other illicit drug use. However, tobacco was the most commonly used substance on a daily basis, whereas marijuana was the most commonly used illicit drug overall. The Monitoring the Future survey<sup>12</sup> and the NSDUH<sup>11</sup> both reported trends and patterns of use for other illicit drugs such as methamphetamines, club drugs (e.g., ketamine, lysergic acid diethylamide [LSD], and methylenedioxymethamphetamine [ecstasy]), and prescription medications. Illicit drug use among adolescents has decreased over the past several years with the exception of prescription medications.

## **OVERLAP AND COMORBIDITIES**

#### Substance Use Disorder in Adults With ADHD

People with ADHD commonly have comorbid disorders such as antisocial disorders, mood disorders, anxiety disorders, and SUDs. Biederman<sup>13</sup> found that almost 30% of adults with ADHD also met the DSM-IV criteria for alcohol and drug dependency. More men than women met the criteria for alcohol and drug dependency, which supports the gender discrepancies found in the NSDUH.<sup>11</sup> An earlier study by Biederman and colleagues<sup>14</sup> compared the prevalence of lifetime psychopathology in adults with and without ADHD (Figure 2). The rates of drug abuse and dependence increased almost 4-fold in adults with ADHD compared with adults without ADHD.

The presence of ADHD may affect the age at onset for SUD. Wilens and colleagues<sup>15</sup> examined the age at onset for SUD in adult patients with untreated ADHD and found that adults with ADHD had a significantly







Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

younger age at onset of SUD compared with patients without ADHD ( $p \le .05$ ). In the past, the presence of conduct disorder or antisocial personality disorder was thought to be responsible for the comorbid association between ADHD and SUD. However, the age at onset for SUD was younger in adults with ADHD regardless of additional psychopathology.<sup>15</sup>

#### ADHD in Adults With Substance Use Disorders

While SUDs are highly prevalent in adults with ADHD, ADHD is conversely overrepresented in patients with SUDs. Wilens<sup>16</sup> reviewed studies of polydrug use, opiate use, cocaine use, and alcohol use and found that, depending on the sample, the rate of ADHD in people with SUDs ranged from 10% to 71%. Kessler and colleagues<sup>17</sup> showed results of the National Comorbidity Survey Replication, which reported that the average prevalence rate of ADHD in patients with SUDs was 10.8% versus only 3.6% in patients without any comorbid disorder.

Several studies<sup>18–21</sup> have examined the influence of ADHD on the severity of SUD. Adults with SUD and comorbid ADHD are more likely than those without co-morbid ADHD to continue to have problematic abuse,<sup>18</sup> and they take longer to achieve remission from SUD.<sup>20</sup> Further, adults with SUD and comorbid ADHD have poorer outcomes than those without ADHD despite more treatment exposure,<sup>18,19,21</sup> suggesting that the presence of ADHD worsens the prognosis for SUD treatment. Patients with SUD and comorbid ADHD also have higher rates of other comorbid disorders than patients with SUD alone.<sup>18,19,21</sup>

## SUBSTANCE MISUSE AND DIVERSION

Medication misuse occurs when the medication is used in a manner in which it was not prescribed. Performance enhancement and recreational use of medication are forms of misuse. However, in order for recreational use to be considered abuse, it must meet the DSM-IV<sup>10</sup> threshold for abuse. The one-time recreational use of a medication to get high does not qualify as abuse. Diversion is the transfer of medication from the patient to another person for any purpose, such as performance enhancement or recreational use. The term *nonmedical use* is often used as a blanket term for misuse, abuse, and diversion.

#### Misuse of Stimulants in the General Population

McCabe and colleagues have published several studies<sup>22-24</sup> on medication diversion and misuse among high school and college students, which showed that the misuse of stimulants in the general population of high school students nearly doubled from 8th grade to 12th grade. A student's academic performance was inversely linked to the misuse of prescription stimulants.<sup>22</sup> Students who made A grades on average had substantially lower misuse of prescription stimulant medications compared with those who were making poorer grades. These data are consistent with reports from the Monitoring the Future survey,<sup>12</sup> which found that the overall use of drugs was lower among high school students who had plans to go to college, which suggests that goal-oriented, long-term plans may be an important protective factor for preventing drug use.

McCabe et al.<sup>23</sup> published a later study of stimulant misuse in college students and found rates similar to those of the high school students in their earlier study.<sup>22</sup> Another important finding from the later study was that universities or colleges with more competitive admissions policies had a higher misuse of stimulant medications than the less competitive schools, which would suggest that these students may be using stimulants for performance enhancement.

#### Misuse and Diversion in the ADHD Population

Students misuse stimulant medications for various reasons. My colleagues and  $I^{25}$  found that 22% of college students prescribed stimulants misused their medication for recreational reasons. In a study conducted by McCabe and colleagues,<sup>24</sup> a substantial minority (5.4%) of students prescribed stimulant medication reported illicitly using their medication. Students who were prescribed stimulant medication at twice the rate (54%) compared with students overall (27%) and students prescribed pain medication (26%) and almost 3 times more (54%) than those prescribed sedatives or anxiety agents (19%) or sleeping medications (14%). Hence, stimulant medications are

Study	N	Drug of Abuse	Study Method	Medication Used	Results
Khantzian <sup>28</sup>	1	Cocaine	CR	Methylphenidate	+
Khantzian et al29	3	Cocaine	CR	Methylphenidate	+
Cocores et al <sup>30</sup>	4	Cocaine	CR	Bromocriptine	+
Cocores et al <sup>31</sup>	2	Cocaine	CR	Bromocriptine	+
Cavanagh et al <sup>32</sup>	2	Cocaine/THC	DB	Bromocriptine	-
Schubiner et al <sup>33</sup>	3	Alcohol	CR	Methylphenidate/dextroamphetamine	+
Levin et al <sup>34</sup>	10	Cocaine	Open	Methylphenidate	+
Schubiner et al <sup>35</sup>	48	Cocaine	DB	Methylphenidate	±
Upadhyaya et al <sup>36</sup>	10	Alcohol/cocaine	Open	Venlafaxine	+
Levin et al <sup>37</sup>	11	Cocaine	Open	Bupropion	+
Vaiva et al <sup>38</sup>	1	Opiates	CR	Moclobemide	+
Riggs et al <sup>39</sup>	69	Various	DB	Pemoline	±
Solhkhah et al <sup>40</sup>	14	Various	Open	Bupropion	+
Carpentier et al <sup>41</sup>	25	Various	DB	Methylphenidate	±
Levin et al42	98	Methadone/cocaine	DB	Methylphenidate/bupropion	-
Levin et al43	106	Cocaine	DB	Methylphenidate	±

Table 1. Studies on the Pharmacologic Treatment of Attention-Deficit/Hyperactivity Disorder and Substance Use Disorder

Abbreviations: CR = case report, DB = double-blind, THC = tetrahydrocannabinol.

Symbols: + = improvements in both attention-deficit/hyperactivity disorder and substance use disorder symptoms,

- = no improvement, and  $\pm$  = mixed results.

desired among college students, perhaps more than analgesics or anxiolytics.

Teter and colleagues<sup>26</sup> found that, of more than 9000 surveyed college students, lifetime prevalence of prescription stimulants was 5.4%. The most frequently reported reasons for stimulant misuse were related to performance enhancement ("helps me concentrate" [58%], "increases my alertness" [43%]). Recreational use was the second most common reason (43%) for illicit use of prescription medication.

Misuse and diversion of stimulant medications arouse safety concerns primarily because there is little or no physician oversight. Without oversight, patients and other stimulant users are at an increased risk for overdose, especially if they are misusing their stimulant medications with other stimulant drugs, such as cocaine. Interactions with nonstimulants may also exist, but without physician oversight, users are often not aware of the contraindications or warnings, including cardiovascular risks in some patients, particularly those with congenital cardiac anomalies.

## Misuse of Immediate-Release Versus Extended-Release Stimulants

Many clinicians report that, according to their patients, extended-release preparations of stimulant medications are more difficult to misuse than immediate-release stimulant medications. Additionally, a recent study<sup>27</sup> found that patients reported that they liked the drug effect more with an immediate-release preparation than the extended-release stimulant, indicating that immediate-release preparations may have greater abuse potential.

Spencer and colleagues<sup>27</sup> randomly assigned 12 patients to comparable oral therapeutic doses of either immediate-release methylphenidate or extended-release methylphenidate. On 2 separate occasions, the patients were questioned on the likeability of the drug. The immediate-release formula was associated with a greater likeability than the osmotic-release formula from 1 to 5 hours after administration. These findings suggest that the extended-release formula of methylphenidate is associated with a lower abuse potential because of its lower likeability ratings, although these results cannot be generalized to other stimulant products.

## TREATMENT OF ADHD IN PATIENTS WITH SUBSTANCE USE DISORDERS

The dilemma that many psychiatrists and primary care physicians face is that the most effective treatments for ADHD—stimulants—also have abuse potential. Treating patients with ADHD and comorbid SUD can be challenging. Unfortunately, not many studies on the treatment of comorbid ADHD and SUD exist (Table 1),<sup>28–43</sup> and initial studies in this area were mainly case reports and case series.<sup>28–31,33</sup> However, more recent studies<sup>34–43</sup> have more subjects and examine a wider range of medications.

Of all of the studies published in the literature, 6 were double-blind, placebo-controlled studies.<sup>32,35,39,41-43</sup> A single<sup>39</sup> study used an adolescent sample, but the study drug, pemoline, is no longer commonly used for ADHD treatment because of its association with liver toxicity. Of the adult studies, 2 examined the effects of methylphenidate on cocaine abuse,<sup>35,43</sup> and 1 examined the effects of methylphenidate and bupropion in patients on methadone maintenance.<sup>42</sup> None of the 4 adult double-blind studies found overall improvement in substance abuse symptoms, but 1 study<sup>43</sup> did suggest that methylphenidate may be associated with a reduction over time of cocaine use. Levin and colleagues<sup>34</sup> found that, in adults with ADHD and comorbid cocaine dependence, methylphenidate was asso-

ciated with a reduction in ADHD symptoms only on the clinician-rated measure. No evidence of ADHD symptom reduction was found on combined measures in this study. Similarly, Riggs and colleagues<sup>39</sup> found significant improvement (p = .05) on the Clinician's Global Impressions-Improvement (CGI-I) for the intent-to-treat sample but no significant improvement (p = .13) on the parent-rated Conners' Hyperactivity-Impulsivity (CHI) scale. In the completer sample the improvement was reversed. Those who finished the 12-week trial had significant improvement (p = .01) on the CHI but not on the CGI-I (p = .24). None of the studies found serious adverse events as a result of treatment, nor did the substance use disorder worsen because of use of a stimulant product. Although none of the studies specifically inquired about diversion behaviors in the samples, none of them reported evidence of diversion.

Several studies<sup>44-47</sup> examined the treatment of cocaine addiction with dextroamphetamine, hypothesizing that substituting a stimulant medication for an illicit stimulant drug could reduce cocaine use. All 4 double-blind, randomized, placebo-controlled trials found that dextroamphetamine treatment reduced cocaine use in the study. However, 2 studies<sup>44,45</sup> found that only higher doses of dextroamphetamine treatment (30-60 mg compared with 15–30 mg) were effective in reducing cocaine dependence. None of the studies reported serious adverse events from amphetamine treatment, and none reported evidence of diversion or misuse of prescribed stimulants. The fact that only the higher doses of dextroamphetamine were able to reduce cocaine use may suggest that the stimulant medications used at lower doses for the treatment of ADHD may be less likely to have cocaine-like effects.

Wilens and colleagues<sup>5</sup> analyzed the literature on whether stimulant treatment for ADHD can lead to SUD in later life. The authors concluded that stimulant medication does not increase the odds of a patient with ADHD having SUD later in life and suggested that stimulant treatment may even have a protective effect.

### CLINICAL CONSIDERATIONS AND RECOMMENDATIONS

Clinicians should approach the treatment of patients with SUD and comorbid ADHD by making a careful assessment using DSM-IV criteria when diagnosing ADHD in patients with SUD. An adequate assessment can help to minimize common problems of overdiagnosis and underdiagnosis of ADHD in patients with SUD.

## Factors Leading to Underdiagnosis of ADHD in Patients With Substance Use Disorder

One factor that may lead to underdiagnosis of ADHD in adults may be the inability to recall symptoms prior to 7 years of age. With these adults, finding a collateral informant (e.g., a parent) who can provide collaborative information about childhood is often difficult. However, patients often may not remember their symptoms prior to 7 years of age, and this is one of the key diagnostic criterion for ADHD.

Another factor leading to underdiagnosis is that some clinicians assume that other psychiatric disorders, such as bipolar disorder or major depressive disorder, preclude the diagnosis of ADHD, and that is not true. For example, a patient can have both bipolar affective disorder and ADHD, but the diagnosis of ADHD becomes harder because of an overlap of symptoms. In addition, the clinician may not use the DSM-IV criteria or a rating scale for diagnosis and instead try to rely on memory to do an assessment for ADHD.

Clinicians often do not recognize that in adults, symptoms of ADHD may be fewer or less obvious than in children. Adults with ADHD often compensate for their ADHD symptoms. For example, college students with ADHD may make good grades, but they may have to study much longer compared with students without ADHD.

# Factors Leading to Overdiagnosis of ADHD in Patients With Substance Use Disorder

Overdiagnosis of ADHD in adult patients with SUD could be avoided if clinicians obtained an adequate longitudinal history. ADHD does not occur de novo in adulthood. It is a developmental disorder, and onset occurs during childhood. A longitudinal history could uncover which patients have a greater likelihood of adult ADHD. Relying on screening instruments alone may also lead to overdiagnosis. ADHD is a clinical diagnosis, and screening instruments can be used as an adjunct tool in the diagnostic process, but the clinician should not substitute these instruments for the valuable diagnostic tool of face-to-face interviews with the patient. Clinicians may fail to ensure that a patient's ADHD symptoms occur in more than 1 setting. ADHD is not a disorder that only occurs at a particular time of day or in a particular setting; it occurs across different settings and throughout the day. Not ensuring that symptoms cause impairment can also lead to the overdiagnosis of ADHD in patients with SUD.

Patients may intentionally exaggerate their symptoms of ADHD in order to mislead their clinician to obtain secondary gains. Exaggerating symptoms can lead to overdiagnosis. Some patients, particularly high school students or college students, may desire special consideration at school, such as extra time on tests, or they may want stimulant medications for misuse or diversion. Keeping in mind what a patient has to gain from an ADHD diagnosis can encourage a clinician to ask the appropriate questions to solidify an accurate diagnosis.

## Evaluating ADHD and

#### Substance Use Disorder in Clinical Practice

Distinguishing between current or past SUD is important when evaluating individuals with ADHD and

Table 2. Some	Commonly Used Tools for	Screening Substance
Use Disorder		

CAGE <sup>49</sup>
Have you ever felt the need to
Cut down on drinking, been
Annoyed by others' criticism of your drinking, felt
Guilty about drinking, needed an
Eye-opener drink first thing in the morning?
AUDIT <sup>50</sup>
Alcohol Use Disorders Identification Test
DAST <sup>51</sup>
Drug Abuse Screening Test
DAP Quick Screen <sup>52</sup>
Drug and Alcohol Problem Quick Screen
CRAFFT <sup>53</sup>
Have you ever ridden in a Car driven by someone (including yourself) who was "high" or had been using alcohol or drugs?
Do you ever use alcohol or drugs to <b>R</b> elax, feel better about yourself, or fit in?
Do you ever use alcohol or drugs while you are Alone?
Do you ever Forget things you did while using alcohol or drugs?
Did your family or Friends ever tell you that you should cut down on your drinking or drug use?
Have you ever gotten into Trouble while you were using alcohol or drugs?

comorbid SUD. These 2 groups may require different treatments, so assessing which group the patient fits into is important before prescribing medication for ADHD. If the patient has a history of drug use, establish the patient's period of abstinence from drug use as well as the details of the patient's treatment.<sup>16,48</sup> If the patient has current SUD, determine whether the patient is currently involved in substance abuse treatment. Before prescribing stimulants for ADHD treatment, find out if the patient has a history of stimulant or amphetamine use or abuse.<sup>48</sup> Patients who have used stimulant medication for performance enhancement may not necessarily need to be excluded from stimulant medication treatment, but those who have used stimulants recreationally should probably not be prescribed stimulant medication first line. Addressing any additional comorbid disorders that may be present is also important because these disorders may require additional medication or treatment.

*Screening tools.* Many tools are available for screening SUDs in adults as well as adolescents (Table 2).<sup>49–53</sup> The CAGE<sup>49</sup> questionnaire (see Table 2 for definition of acronym) is a commonly used screening tool. It is a 4-item questionnaire asking if the patient has ever felt the need to cut down on drinking, been annoyed by others' criticism of their drinking, felt guilty about drinking, or needed an eye-opener drink first thing in the morning. For adolescents, the CRAFFT<sup>53</sup> questionnaire (see Table 2) is the recommended screening tool. The CRAFFT questionnaire has good sensitivity (92.3%) and specificity (82.1%) for identifying adolescents needing alcohol and other drug treatment.

*Toxicology tests.* Toxicology tests are a key component of assessment and treatment of substance use disorders.

Toxicology tests that show ranges of detection of various drugs in the urine can be used to determine the length of time between ingesting a drug and when the drug can be detected in the urine.<sup>54</sup> Toxicology tests can be helpful in detecting substance use or abuse in patients. If a clinician suspects that a patient is using illicit drugs during treatment, the frequency of urine tests can be determined by gauging the amount of time it would take for the suspected drug of use to be eliminated from the patient's system.

## Clinical Recommendations for Treating ADHD in Patients With Substance Use Disorder

The use of stimulant medication in substance-abusing patients is complex and controversial. If possible, clinicians should include family members or close non–substance-using friends in the treatment plan to monitor the patient and to provide useful information. Inform the patient and family of potential risks involved in using stimulants. For patients actively using drugs or for those who are only recently abstinent, consider using nonstimulants as first-line treatment.<sup>16,48,55</sup> Each one of the non-stimulants should be considered individually for treatment based on its benefits to the patient.<sup>55</sup> For example, because of its antianxiety properties, atomoxetine may be a preferred product if a patient has a comorbid anxiety disorder.

Precautionary steps can be taken in clinical settings when using medications with abuse potential in patients with ADHD and comorbid SUD. The first precautionary step is to limit and keep track of pills by having the patient bring the pill bottle at each visit. Second, obtain urine toxicology screens at regular patient visits to monitor substance use in general. Frequent visits are important; seeing a patient with ADHD once a month is not unusual, and tracking prescription medication improves patient compliance. Third, prescribing long-acting preparations of stimulant medications, such as osmotic release oral system methylphenidate and lisdexamfetamine dimesylate, which is an amphetamine-prodrug, may be desirable. The methylphenidate transdermal patch also has properties that make it harder to abuse. Nonpharmacologic approaches for ADHD may also be explored in adults, such as cognitive remediation and cognitive-behavioral therapy. Fourth, emphasize the importance of taking medications regularly, not on an as-needed basis. Some patients do not take their medications daily and then divert or misuse the leftover medication. Finally, discuss with patients how to store the medication safely and avoid letting others know that they are taking a stimulant medication.

Red flags for diversion or misuse include patients demanding immediate-release products, having repeatedly discordant pill counts, frequently losing prescriptions and calling for another one, and frequently asking to escalate the dose. Symptoms of psychosis can be a red flag for misuse, but they can also mean that patients are having side effects from the medication. Symptoms associated with heavier-than-prescribed use include palpitations, syncope, and shortness of breath.

Having an intervention plan for patients with ADHD and comorbid SUD is an important part of managing the comorbidity. Be aware of the resources for SUD treatment in the community, know the risks of stimulant medication use, and warn patients about the consequences of misuse and diversion. Frequently monitor the patient's ADHD response with rating scales, schedule more frequent office visits to monitor medication usage and drug abuse, and involve the family in the treatment process. Consider using a stimulant medication for a patient who has a documented history of sobriety, but if the patient is actively using a drug, consider delaying the use of stimulant medication until the SUD is in remission. Office-based or laboratory toxicology testing can be used as indicated. Assess the family for SUD and refer them for treatment if necessary. Optimally, efficacious treatment strategies for SUD should be used in an integrated fashion with ADHD treatment to treat patients with both ADHD and SUD. Efficacious psychosocial treatment strategies for SUD include cognitive-behavioral therapy, contingency management, the 12-step Minnesota model, motivational interviewing, family therapies, and combination therapies, such as integrative psychosocial therapy. Pharmacotherapy for specific substances (e.g., naltrexone for alcohol dependence) should be considered.

### CONCLUSION

ADHD is present in a substantial proportion of substance-abusing people seeking treatment, and ADHD is an independent risk factor for SUD. Additional psychiatric comorbidities are common in individuals with ADHD and should be considered when developing a plan to treat not only the ADHD symptoms but comorbid SUD as well. The treatment of individuals with ADHD and comorbid SUD requires management of both the SUD and ADHD symptoms in an integrated fashion, not as separate entities.

*Drug names*: atomoxetine (Strattera), bromocriptine (Parlodel and others), bupropion (Wellbutrin and others), dextroamphetamine (Dextrostat, Dexedrine, and others), lisdexamfetamine (Vyvanse), methylphenidate (Methylin, Ritalin, and others), naltrexone (ReVia and others), osmotic release oral system methylphenidate (Concerta), transdermal methylphenidate (Daytrana), venlafaxine (Effexor and others).

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, bromocriptine and dextroamphetamine are not approved by the U.S. Food and Drug Administration for the treatment of cocaine use disorder and bupropion and venlafaxine are not approved for the treatment of attention-deficit/hyperactivity disorder. If you have questions, contact the medical affairs department of the manufacturer for the most recent prescribing information.

#### REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC:

American Psychiatric Association; 1994

- American Academy of Pediatrics. Clinical practice guideline: diagnosis and evaluation of the child with attention-deficit/hyperactivity disorder. Pediatrics 2000;105:1158–1170
- Barbaresi WJ, Katusic SK, Colligan RC, et al. How common is attentiondeficit/hyperactivity disorder? incidence in a population-based birth cohort in Rochester, Minn. Arch Pediatr Adolesc Med 2002;156:217–224
- Faraone SV, Biederman J, Mick E, et al. Family study of girls with attention deficit hyperactivity disorder. Am J Psychiatry 2000;157:1077–1083
- Wilens TE, Faraone SV, Biederman J, et al. Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? a meta-analytic review of the literature. Pediatrics 2003;111:179–185
- Katusic SK, Barbaresi WJ, Colligan RC, et al. Psychostimulant treatment and risk for substance abuse among young adults with a history of attention-deficit/hyperactivity disorder: a population-based, birth cohort study. J Child Adolesc Psychopharmacol 2005;15:764–776
- Wilson JJ, Levin FR. Attention-deficit/hyperactivity disorder and earlyonset substance use disorders. J Child Adolesc Psychopharmacol 2005;15: 751–763
- McCabe SE, Teter CJ, Boyd CJ. The use, misuse and diversion of prescription stimulants among middle and high school students. Subst Use Misuse 2004;39:1095–1116
- Wilens TE, Gignac M, Swezey A, et al. Characteristics of adolescents and young adults with ADHD who divert or misuse their prescribed medications. J Am Acad Child Adolesc Psychiatry 2006;45:408–414
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC: American Psychiatric Association; 2000
- 11. United States Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, Office of Applied Studies. 2004 National Survey on Drug Use and Health: National Findings. Rockville, Md: US Department of Health and Human Services; 2004. Available at: http://oas.samhsa.gov/nhsda/2k4nsduh/ 2k4results.htm. Accessed January 4, 2007
- Johnston LD, O'Malley PM, Bachman JG, et al. Monitoring the Future National Survey Results on Drug Use, 1975–2004: Volume 1, Secondary School Students. Bethesda, Md: National Institute on Drug Abuse; 2005. Available at: http://www.monitoringthefuture.org/pubs/monographs/ vol1\_2004.pdf. Accessed January 17, 2007
- Biederman J. Attention-deficit/hyperactivity disorder: a selective overview. Biol Psychiatry 2005;57:1215–1220
- Biederman J, Faraone SV, Spencer T, et al. Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention deficit hyperactivity disorder. Am J Psychiatry 1993;150:1792–1798
- Wilens TE, Biederman J, Mick E, et al. Attention deficit hyperactivity disorder (ADHD) is associated with early onset substance use disorders. J Nerv Ment Dis 1997;185:475–482
- Wilens TE. Attention-deficit/hyperactivity disorder and the substance use disorders: the nature of the relationship, subtypes at risk, and treatment issues. Psychiatr Clin North Am 2004;27:283–301
- Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry 2006;163:716–723
- Carroll KM, Rounsaville BJ. History and significance of childhood attention deficit disorder in treatment-seeking cocaine abusers. Compr Psychiatry 1993;34:75–82
- Schubiner H, Tzelepis A, Milberger S, et al. Prevalence of attentiondeficit/hyperactivity disorder and conduct disorder among substance abusers. J Clin Psychiatry 2000;61:244–251
- Wilens TE, Biederman J, Mick E. Does ADHD affect the course of substance abuse? findings from a sample of adults with and without ADHD. Am J Addict 1998;7:156–163
- Levin FR, Evans SM, Kleber HD. Prevalence of adult attention-deficit hyperactivity disorder among cocaine abusers seeking treatment. Drug Alcohol Depend 1998;52:15–25
- McCabe SE, Teter CJ, Boyd CJ, et al. Prevalence and correlates of illicit methylphenidate use among 8th, 10th, and 12th grade students in the United States, 2001. J Adolesc Health 2004;35:501–504
- McCabe SE, Knight JR, Teter CJ, et al. Non-medical use of prescription stimulants among US college students: prevalence and correlates from a national survey. Addiction 2005;100:96–106
- McCabe SE, Teter CJ, Boyd CJ. Medical use, illicit use, and diversion of abusable prescription drugs. J Am Coll Health 2006;54:269–278

- Upadhyaya HP, Rose K, Wang W, et al. Attention deficit hyperactivity disorder, medication treatment, and substance use patterns among adolescents and young adults. J Child Adolesc Psychopharmacol 2005;15: 799–809
- Teter CJ, McCabe SE, Cranford JA, et al. Prevalence and motives for illicit use of prescription stimulants in an undergraduate student sample. J Am Coll Health 2005;53:253–262
- Spencer TJ, Biederman J, Ciccone PE, et al. PET study examining pharmacokinetics, detection and likeability, and dopamine transporter receptor occupancy of short- and long-acting oral methylphenidate. Am J Psychiatry 2006;163:387–395
- Khantzian EJ. An extreme case of cocaine dependence and marked improvement with methylphenidate treatment. Am J Psychiatry 1983;140: 784–785
- Khantzian EJ, Gawin F, Kleber HD, et al. Methylphenidate (Ritalin) treatment of cocaine dependency: a preliminary report. J Subst Abuse Treat 1984;1:107–112
- Cocores JA, Davies RK, Mueller PS, et al. Cocaine abuse and adult attention deficit disorder. J Clin Psychiatry 1987;48:376–377
- Cocores JA, Patel MD, Gold MS, et al. Cocaine abuse, attention deficit disorder, and bipolar disorder. J Nerv Ment Dis 1987;175:431–432
- Cavanagh R, Clifford JS, Gregory WL. The use of bromocriptine for the treatment of attention deficit disorder in two chemically dependent patients. J Psychoactive Drugs 1989;21:217–220
- Schubiner H, Tzelepis A, Isaacson JH, et al. The dual diagnosis of attention-deficit/hyperactivity disorder and substance abuse: case reports and literature review. J Clin Psychiatry 1995;56:146–150
- Levin FR, Evans SM, McDowell DM, et al. Methylphenidate treatment for cocaine abusers with adult attention-deficit/hyperactivity disorder: a pilot study. J Clin Psychiatry 1998;59:300–305
- Schubiner H, Saules K, Arfken C, et al. Double-blind placebo-controlled trial of methylphenidate in the treatment of adult ADHD patients with comorbid cocaine dependence. Exp Clin Psychopharmacol 2002;10: 286–294
- Upadhyaya HP, Brady KT, Sethuraman G, et al. Venlafaxine treatment of patients with comorbid alcohol/cocaine abuse and attention-deficit hyperactivity disorder: a pilot study. J Clin Psychopharmacol 2001;21:116–118
- Levin FR, Evans SM, McDowell DM, et al. Bupropion treatment for cocaine abuse and adult attention-deficit/hyperactivity disorder. J Addict Dis 2002;21:1–16
- Vaiva G, De Lenclave MB, Bailly D. Treatment of comorbid opiate addiction and attention-deficit hyperactivity disorder (residual type) with moclobemide: a case report. Prog Neuropsychopharmacol Biol Psychiatry 2002;26:609–611
- Riggs PD, Hall SK, Mikulich-Gilbertson SK, et al. A randomized controlled trial of pemoline for attention-deficit/hyperactivity disorder in substance-abusing adolescents. J Am Acad Child Adolesc Psychiatry 2004;43:420–429
- 40. Solhkhah R, Wilens TE, Daly J, et al. Bupropion SR for the treatment of

substance-abusing outpatient adolescents with attention-deficit/ hyperactivity disorder and mood disorders. J Child Adolesc Psychopharmacol 2005;15:777–786

- Carpentier PJ, de Jong CA, Dijkstra BA, et al. A controlled trial of methylphenidate in adults with attention deficit/hyperactivity disorder and substance use disorders. Addiction 2005;100:1868–1874
- 42. Levin FR, Evans SM, Brooks DJ, et al. Treatment of methadonemaintained patients with adult ADHD: double-blind comparison of methylphenidate, bupropion and placebo. Drug Alcohol Depend 2006;81:137–148
- Levin FR, Evans SM, Brooks DJ, et al. Treatment of cocaine dependent treatment seekers with adult ADHD: double-blind comparison of methylphenidate and placebo. Drug Alcohol Depend 2007;87:20–29
- 44. Grabowski J, Rhoades H, Stotts A, et al. Agonist-like or antagonist-like treatment for cocaine dependence with methadone for heroin dependence: two double-blind randomized clinical trials. Neuropsychopharmacology 2004; 29:969–981
- Grabowski J, Rhoades H, Schmitz J, et al. Dextroamphetamine for cocaine-dependence treatment: a double-blind randomized clinical trial. J Clin Psychopharmacol 2001;31:522–526
- Shearer J, Wodak A, Matick R, et al. Pilot randomized controlled study of dexamphetamine substitution for amphetamine dependence. Addiction 2001;96:1289–1296
- Shearer J, Wodak A, van Beek I, et al. Pilot randomized double blind placebo-controlled study of dexampletamine for cocaine dependence. Addiction 2003;98:1137–1141
- Riggs PD. Clinical approach to treatment of ADHD in adolescents with substance use disorders and conduct disorder. J Am Acad Child Adolesc Psychiatry 1998;37:331–332
- Ewing JA. Detecting alcoholism: the CAGE questionnaire. JAMA 1984;252:1905–1907
- 50. Babor TF, de la Fuente JR, Saunders J, et al. The Alcohol Use Disorders Identification Test Guidelines for Use in Primary Health Care. 2nd ed. Geneva, Switzerland: World Health Organization; 2001
- Skinner HA. The drug abuse screening test. Addict Behav 1982;7:363–371
- Schwartz RH, Wirtz PW. Potential substance abuse: detection among adolescent patients: using the Drug and Alcohol (DAP) Quick Screen, a 30-item questionnaire. Clin Pediatr 1990;29:38–43
- Knight JR, Sherritt L, Shrier LA, et al. Validity of the CRAFFT substance abuse screening test among adolescent clinic patients. Arch Pediatr Adolesc Med 2002;156:607–614
- 54. Bukstein OG, Bernet W, Arnold V, et al, for the Work Group on Quality Issues for the American Academy of Child and Adolescent Psychiatry. Practice parameters for the assessment and treatment of children and adolescents with substance use disorders. J Am Acad Child Adolesc Psychiatry 2005;44:609–621
- Schubiner H. Substance abuse in patients with attention-deficit hyperactivity disorder: therapeutic implications. CNS Drugs 2005;19:643–655