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# THE MEDICAL VIEW

## Abuse, Diversion, & Misuse of ADHD Medications

### CME-Certified Activity

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Release Date: September 2006 • Expiration Date: September 30, 2007

This activity is supported by an educational grant from Shire Pharmaceuticals Inc.

# Abuse, Diversion, & Misuse of ADHD Medications

CME Certified Print Monograph/Companion Audio CD



Sponsored by the University of Medicine & Dentistry of New Jersey (UMDNJ)–  
Center for Continuing and Outreach Education

Release Date: September 2006 • Expiration Date: September 30, 2007

This activity is supported by an educational grant from Shire Pharmaceuticals Inc.

## Educational Goal

The overlap between Attention Deficit Hyperactivity Disorder (ADHD) and Substance Use Disorder (SUD) in pediatrics, adolescents, and adults is an area of increasing interest and concern. Although stimulant medications have been shown to be effective in the treatment of adolescents and young adults with ADHD and are associated with a reduction in the risk for subsequent SUDs, a primary concern is that these medications will be misused or diverted to those for whom they have not been prescribed. During this program a panel of well-known experts will address these concerns and issues as they share their views.

## Target Audience

This educational activity strives to meet the educational needs of psychiatrists, pediatricians, primary care physicians, and other health care professionals interested in, or involved in, the management of patients with ADHD.

## Learning Objectives

- Discuss the connection between substance abuse and ADHD in children, adolescents, and adults
- Gain an understanding of abuse, diversion, and misuse among ADHD medications
- Review risk factors for the development of substance abuse disorders in patients diagnosed with ADHD
- Discuss methods for clinicians to decrease abuse liability and insure compliance among patients with ADHD
- Review available agents for treating patients with ADHD and their potential for abuse and diversion, categorizing them by class

## Method of Instruction

Participants should read the learning objectives and review the print monograph, or the audio CD, in its entirety. After reviewing the material, complete the self-assessment test consisting of a series of multiple-choice questions. The activity is complemented with references that contain the rationale for the correct answer to each question as well as a description identifying the section in the activity that contains the correct answer, allowing participants to review the material as needed, thus finalizing their educational participation.

Upon completing this activity participants will receive a letter of credit awarding *AMA PRA Category 1 credit(s)*<sup>TM</sup> four weeks after receipt of the registration and evaluation materials.

Estimated time to complete the print monograph as designed is one (1) hour.

Estimated time to complete the audio CD as designed is one and a half (1.5) hours.

## Accreditation

UMDNJ–Center for Continuing and Outreach Education is accredited by the ACCME to provide continuing medical education for physicians.

UMDNJ–Center for Continuing and Outreach Education designates this educational activity *AMA PRA Category 1 Credit(s)*<sup>TM</sup>. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Abuse, Diversion, and Misuse of ADHD Medications monograph is designated for a maximum of 1 *AMA PRA Category 1 Credit(s)*<sup>TM</sup>.

Abuse, Diversion, and Misuse of ADHD Medications audio CD is designated for a maximum of 1.5 *AMA PRA Category 1 Credit(s)*<sup>TM</sup>.

The print monograph was peer-reviewed for relevance, accuracy of content, and balance of presentation by Tolga Taneli, MD and pilot-tested for time required for participation by Jeffrey Aronowitz, DO and John F. Schiltz, MD, PhD. The audio presentation was peer-reviewed by Tolga Taneli MD, and pilot tested by Edward Phinney, MD and Elena Volfson, MD, MPH.

## Disclosure Declarations

In accordance with the disclosure policies of UMDNJ and to conform with ACCME and FDA guidelines, individuals in a position to control the content of this education are required to disclose to the activity participants: 1) the existence of any financial interest or other relationships with proprietary entities producing health care goods or services, with the exemption of non-profit or government organizations and non-health care related companies, within the past 12 months; and 2) the identification of a commercial product/device that is unlabeled for use or an investigational use of a product/device not yet approved.

## Faculty Disclosure Declarations

### *Joseph Biederman*

Grants/Research Support: Abbott Laboratories, Alza/Ortho-McNeil Pharmaceuticals, Bristol-Myers Squibb Company, Cephalon, Eli Lilly and Company, Janssen, Lilly Foundation, NeuroSearch, New River Pharmaceuticals, NICHD, NIDA, NIMH, Novartis, Pfizer, Prechter Foundation, Shire US, and The Stanley Medical Research Institute; Consultant: Alza/Ortho-McNeil Pharmaceuticals, Cephalon, Eli Lilly and Company, Janssen, Novartis, and Shire US; Speaker's Bureau: Alza/Ortho-McNeil Pharmaceuticals, Cephalon, Eli Lilly and Company, Novartis, Shire US, and UCB Pharma.

### *William W. Dodson*

Consultant: Shire US; Speaker's Bureau: Novartis and ShireUS.

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Dr. Salgo has no financial arrangement or affiliations to disclose.

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Dr. Taneli has no financial arrangement or affiliations to disclose.

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It should be noted that the recommendations made herein with regard to the use of therapeutic agents, varying disease states, and assessments of risk, are based upon a combination of clinical trials, current guidelines, and the clinical practice experience of the participating presenters. The drug selection and dosage information presented in this activity are believed to be accurate. However, participants are urged to consult the full prescribing information on any agent(s) presented in this activity for recommended dosage, indications, contraindications, warnings, precautions, and adverse effects before prescribing any medication.

# Abuse, Diversion, & Misuse of ADHD Medications

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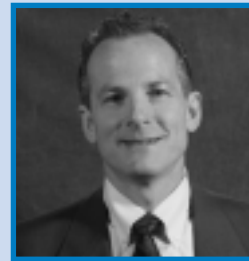
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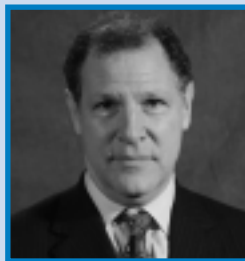
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**T**he CNS stimulant medications, methylphenidate and amphetamines, used for the treatment of patients with attention-deficit/hyperactivity disorder (ADHD), produce their CNS stimulant effect by binding to presynaptic dopamine receptors, thus increasing dopamine activity in brain synapses.<sup>1</sup> Enhancement of dopamine pathways are associated with reinforcing (manifested as the “high”) and rewarding effects that promote addiction.<sup>2</sup>

The overlap between ADHD and substance use disorders (SUDs) in pediatric, adolescent, and adult patients is an area of increasing interest and concern. Studies have shown that 20% to 30% of adults presenting with SUD have concomitant ADHD and approximately 20% to 40% of adults with ADHD have a previous history of SUD.<sup>1</sup> It also appears that patients of all age groups tend to manifest symptoms of ADHD earlier than SUDs (ie, in the majority of cases, symptoms of ADHD precede signs of abuse disorder).<sup>3</sup> Adults with SUDs, in comparison to other age groups, tend to display an earlier onset and more severe course of SUD in association with the manifestation of ADHD.<sup>4,5</sup> Although stimulant medications have been shown to be effective in the treatment of adolescents and young adults with ADHD and are associated with a reduction in the risk for subsequent SUDs,<sup>6</sup> a primary concern is that these medications will be misused or diverted to those for whom they have not been prescribed. When prescribing pharmacotherapy for individuals with ADHD and SUD, the physician should consider abuse liability, potential drug interactions, and concerns regarding compliance.<sup>3</sup> In this Medical View, a panel of experts discusses various aspects of abuse, diversion, and misuse of CNS stimulants used to treat ADHD, including strategies to reduce abuse potential.

## Abuse Potential of CNS Stimulants

Moderator Peter Salgo, MD, began the program by asking the panelists if there are different abuse potentials among stimulant medications. “Although there are 16 FDA-approved brand name products that are considered to be first-line medications for the treatment of ADHD, these products are different formulations of only 2 compounds, methylphenidate and amphetamine”, responded William Dodson, MD. “The stimulant medications used in the treatment of ADHD have abuse potential, as evidenced by their FDA classification as a Class II drug. As a class, these CNS stimulants all have a similar abuse potential.”<sup>7</sup>

“Despite the fact that these medications are probably the most prevalent prescription medications used for treating schoolchildren, and high school- and college-aged individuals, their misuse and abuse is very low,” interjected Dr. Dodson. “Their low abuse potential is supported by findings of 2 large in-depth surveys of college students with sample sizes of approximately 9,000<sup>8</sup> and 10,000<sup>9</sup> students, respectively. These surveys found that the 1-year rate of non-medical or illicit use of prescription stimulants is only about 4%<sup>8</sup> or 5%.”<sup>9</sup>

Timothy Wilens, MD, added a final caveat regarding the assessment of abuse or misuse potential of a CNS stimulant in a given individual: “When you’re evaluating the literature it’s helpful to know what paradigm was used in abuse liability assessment. Some studies examined abuse liability in a non-addicted study population with no prior exposure to stimulants. In contrast, other studies have shown that the study population consisted of individuals with a history of substance abuse, such as those individuals with previous cocaine-dependency.”

## Short-Acting vs Long-Acting Stimulants: Differences in Abuse Potential

In response to the question: “Are there any differences in abuse potential between short- and long-

acting stimulants?” posed by Dr. Salgo, Dr. Goodman remarked, “In order to get high from stimulants, there has to be a rapid increase in blood levels.<sup>10,11</sup> Therefore, the greatest abuse is likely to occur with agents with short durations of action, the reason being that they can be crushed, and the powder either snorted or dissolved in water and injected intravenously.” These latter routes of drug intake result in rapid delivery to the brain and rapid onset of action/euphoria.<sup>11-13</sup> “The long-acting medications have less abuse potential because they are not as amenable to being crushed and snorted,”<sup>14</sup> said Dr. Biederman.

Dr. Wilens added, “Data from recent publications that compared the behavioral effects of extended-release and immediate-release formulations of a stimulant (methylphenidate), given in equal daily doses,<sup>13</sup> indicate that the longer it takes for the medication to reach the site of action in the brain, in this case, the dopamine transporter,<sup>15</sup> the less people feel the ‘good effects’ of the medication and the less likely they are to abuse the medication.”<sup>11</sup>

Dr. Wilens then discussed findings from his recent questionnaire-based study in which he examined self-reported misuse and diversion (eg, selling) of ADHD medication among 98 young male adults (mean age, 21 years), all of whom had a diagnosis of conduct disorder or substance abuse disorder.<sup>16</sup> In this group, 55 subjects had ADHD. Only short-acting formulations of ADHD medications were misused or diverted. There was no misuse or abuse of long-acting formulation. “Thus, we would then expect a lower likelihood of misuse or diversion of the extended-release formulations compared to the immediate-release formulations. So I wouldn’t say that the extended-release types of medication are totally void of any misuse or diversion potential, but it certainly seems they are a lot less than the immediate-release preparations.” It should be noted, however, that the data suggesting a decreased abuse potential with extended-release formulations is limited by a bias potential since studies have not controlled for a lower volume of prescriptions in comparison to immediate-release formulations.

## Comorbid Psychiatric Risk Factors for Abuse Liability

“I would now like to discuss the important psychiatric risk factors that will increase abuse potential with ADHD treatment,” requested Dr. Salgo. “It is well known that individuals with ADHD who also have other co-occurring problems are at higher risk for substance use disorders,” responded Dr. Wilens. “In particular, patients who have ADHD plus conduct disorder or bipolar disorder are at an increased risk for substance use disorders.<sup>17</sup> Furthermore, ADHD patients tend to be somewhat disorganized in terms of taking their medications, and if they are prescribed stimulant medications, they might be at a higher risk for misusing them.”

“Bipolar disorder and ADHD are often found together”, remarked Dr Dodson. The STEP-BD (Systematic Treatment Enhancement Program for Bipolar Disorder) – a multicenter project funded by the National Institute of Mental Health that was designed to evaluate the longitudinal outcome of patients with bipolar disorder – found that 9.5% of the bipolar disorder sample also had a lifetime diagnosis of ADHD.<sup>18</sup> “Personal communications I have had with Dr Nierenberg indicate that this percentage may be as high as 25%, but that is unsubstantiated by published clinical studies. Also, approximately 25% to 30% of individuals with substance abuse disorder have ADHD.”<sup>19,20</sup>

“There is a high degree of psychiatric comorbidity with ADHD”, confirmed Dr Goodman.<sup>21,22</sup>

“Therefore, the increased risk of substance abuse in an individual with ADHD and comorbid bipolar disorder, depression, or anxiety disorder, stresses the point that not only should the ADHD be identified and treated as soon as possible, but the psychiatric comorbidities should also be treated.”

## Decreasing Abuse Liability

“What can clinicians do to decrease abuse liability?”, asked Dr. Salgo. “The most important thing that a clinician can do is perform a good evaluation

of the patient.” replied Dr. Dodson. “People who are going to misuse ADHD medications are usually identifiable. They are not your average ADHD patients.” Dr. Dodson and Dr. Wilens characterized people at risk for abusing or misusing ADHD medications as those with “oppositional defiance, delinquency or conduct disorder, established substance use disorder, history of misusing other types of compounds, including other prescription medications, or tendency to experiment with cocaine and other substances.”<sup>8,14,22,23</sup> “Studies looking at college students also identified white male members of a fraternity as a risk group for illicit use and diversion of prescription stimulants,” added Dr. Dodson.<sup>24</sup>

Dr. Wilens remarked that “clinicians can stay on top of the abuse, misuse or diversion of medications by first talking about it with patients, parents, and teachers, and stating up front that they are conscious of issues around the proper use, storage, and administration of the medication. For high risk patients, I make it clear to them that I am only going to issue monthly prescriptions of the medication and carefully monitor pill counts. If they request medication at an increased frequency beyond what I expect based on their daily dose, then I’ll call it into question and have them come back to talk about proper use of the medicine. Other things that can be done are: to advise patients/parents to keep the medications safely stored in clothes drawers rather than medicine cabinets, which is where people typically look for substances of abuse; rotate storage location and not publicize the fact that they are on stimulant medications; and ensure that the individual is taking the medication as prescribed. Individuals should also be made to understand that if they’re having difficulties during certain periods of the day, they need to discuss with you the appropriate dose titration; they are not to make these decisions on their own. Otherwise, they may escalate the dose to the point where it’s at a very high dose and puts them at risk for misuse.” Another strategy to decrease abuse liability is to use forms of medications that we think are being less misused and diverted, such as the extended-release form of stimulants as opposed to the immediate-release form.”

Dr. Goodman expanded this point by commenting that, “we can decrease abuse liability by diminishing and limiting the amount of short-acting stimulant medications available amongst our patients, families, and the community at large. In treating ADHD patients, we should use the longer-acting once-a-day stimulant regimens as the first choice and first line treatment before turning to short-acting preparations.”

## Identifying Abuse, Diversion and Misuse of ADHD Medications

“What can clinicians do to identify diversion and abuse?”, asked Dr. Salgo. “The first thing they need to do is clarify terminology”, responded Dr. Dodson. A person with ADHD who has not been evaluated but is using someone else’s medication because they find it improves their functioning can be said to misuse the medication. This person should be evaluated for ADHD and given his/her own prescription. A person who uses the medication in a way that is not approved by the FDA, eg, to stay up all night, is also guilty of misuse. People who abuse drugs in general and use the medication as part of an abusive pattern are guilty of abuse. It is important to ascertain the individual’s intent.” “Identifying individuals at risk for diversion and abuse (eg, individuals with conduct disorder, oppositional defiant disorder, juvenile delinquents, and arrest records) and careful monitoring of patients and prescriptions is important,” added Dr. Goodman.

## Responding to Apparent Abuse, Diversion, or Misuse

“When you identify diversion or abuse, how do you alter treatment?”, asked Dr. Salgo. “If I suspect diversion or misuse, or drug or alcohol abuse, or if I get a concerned call from a parent or a friend, I call the individual back for a visit”, said Dr. Wilens. “I discuss with the individual the concerns of proper use of the medication and ask point blank if he or she is using the medications exactly as indicated. If not, a discussion follows. If I have a stronger indication that, in fact, they may be misusing or diverting the medication, then I talk to them about ancillary treatments for ADHD, and about the ramifica-

tions of misusing or diverting medication, such as being expelled from university and/or being incarcerated for drug trafficking. By using extended-release as opposed to immediate-release treatment forms, we can reduce this as a college problem.”

“Treatment for ADHD will have to stop and the patient will need to be treated for diversion, abuse, or misuse of the medication”, said Dr. Biederman. “This setting is not a safe environment to treat ADHD.” Dr. Dodson added that once the substance abuse is under control and the individual is in a recovery program, “often I will start that person out again on a second-line non-stimulant agent that has virtually no abuse potential. The one that is FDA-approved is Atomoxetine HCl, although there are other effective medications that are not FDA-approved for ADHD, such as bupropion.” “Do the available published data support the need for caution when prescribing therapies for ADHD that have high abuse potential?”, asked Dr. Salgo. Dr. Wilens commented that, “many published studies have provided evidence that there is diversion and misuse of stimulant-class agents among high school and college-age students.<sup>1</sup> Most of it is in the form of individuals taking the medicine to help them with studying, to keep them awake, to be able to complete projects – some of whom may have coincident ADHD or neuropsychologic problems anyway. This problem has existed since the 1970s when the isomeric form of amphetamine was commonly used for weight control. While the potential problem of abuse/misuse/diversion is an issue that we need to be aware of, it should not significantly alter our diagnosis or treatment of ADHD, but should be addressed with potentially vulnerable individuals.”

“We prescribe a lot of medications that have abuse potential, such as benzodiazepines, sedative hypnotics, and pain medications, on a daily basis,” added Dr. Dodson. “In the case of ADHD medications, we simply have to use the same clinical judgment that we use in those situations. In point of fact, ADHD medications were not controlled substances until 1978. Amphetamine was on the market as an over-the-counter medication for more than 80 years before it was even made a prescrip-

tion medication and for another 20 years before it was made a controlled substance. We have a lot of experience with these medications. But the real problem is that clinicians often don’t prescribe stimulant medications out of fear that they might be misused. As a result, the individual with ADHD may not receive proper treatment.”

## Treatment Decisions in Patients with History of SUD

“How should a history of SUD affect treatment decisions for ADHD?”, asked Dr. Salgo. Dr. Wilens responded by emphasizing that, “it is critical to ascertain the patient’s past substance use history. Do they have a past history of alcohol or other substance use disorders? If so, what is the proximity of that problem to the present situation? For example, is it something that occurred 10 or 15 years ago and you are now treating somebody who is relatively free of any type of SUD history in the last 10 years? For an individual fitting this scenario, you can choose any treatment for ADHD without major concern for addiction. In contrast, an individual with a relatively recent SUD history, eg, within the previous 3 months, must be assessed carefully. Is this person truly stable with their substance use? If so, I am going to use a non-stimulant class agent like atomoxetine or bupropion. If I decide to use a stimulant, I’m definitely going to monitor the patient carefully for proper use and diversion and to prescribe one of the extended-release formulations of either methylphenidate or amphetamine. For an individual with current, active substance use history, eg, alcohol or drug abuse, the first step is aggressive treatment of the addiction followed by treatment of the underlying ADHD in rapid succession, in part to help keep that individual involved in their addiction treatment. In this individual, a non-stimulant agent should definitely be used initially. If non-stimulant treatment is not successful or cannot be used, a stimulant can be used, but should start with the extended-release formulation.”

Dr. Dodson emphasized the importance of careful history taking in an individual presenting with SUD history. “I ask the question, ‘When you used

your substance, what were you looking for?’ If the person gives any indication of euphoric recall (ie, enjoying the “high”), I’m going to use a second-line agent. If, on the other hand – and this is by far, the most common reason – the person was looking for adaptive functioning (eg, ‘slowing my brain down enough to fall asleep or to study’), this person is a reasonable candidate for a first-line agent, although prudent precautions should be used. For example, a responsible significant other should be in control of the medication; a supportive environment should be ensured; and there should be a clear understanding that you’re going to do random, unannounced urine drug screens.”

## Consequences of Not Treating ADHD

“What are the consequences for ADHD patients who go untreated?”, asked Dr. Salgo. “Untreated ADHD has a negative impact on individual’s lives, both quantitatively and qualitatively. It brings with it a whole host of difficulties ranging from academic underachievement, occupational underachievement, difficulties with social relationships, increased utilization of healthcare systems, motor vehicle accidents, high-risk behaviors, and unwanted pregnancies”, replied Dr. Wilens.<sup>25,26</sup> Dr. Dodson added that, “people with untreated ADHD are far more likely to drop out of school, have poor work performance and employment records, have failed relationships, be involved in injury-producing motor vehicle accidents, and contract a sexually transmitted disease.<sup>26</sup> ADHD is not a benign condition and it impairs everything in life and has ramifications throughout life.” “We need to understand that the treatment of ADHD is so effective, and hopefully will reduce and diminish these poor outcomes for the untreated ADHD patient”, commented Dr. Goodman.

## Compliance

“What role does compliance play in reducing the consequences of untreated ADHD?”, asked Dr. Salgo. “We know that adequacy of treatment seems to be directly related to the long-term prognosis in terms of sequelae of ADHD. A critical component

of treatment adequacy is compliance with treatment,” replied Dr. Wilens.

“The illness is chronic and the symptoms are not curable,” added Dr. Biederman. “Therefore, if the patient is not compliant, the symptoms will re-emerge, as will the dysfunction and morbidity associated with ADHD.” Dr. Goodman emphasized that, “it’s important to teach patients that taking medication on a consistent, daily basis is critical to effective treatment. Compliance in ADHD patients, however, is notoriously poor.”<sup>27</sup> After 9 months, only 15% of patients have continued taking their medications.<sup>28</sup>

## Emerging Therapies and Abuse Potential

“Do emerging therapies for ADHD provide a realistic solution with regard to reduced abuse and diversion potential, while still providing efficacy?”, asked Dr. Salgo. “Some of the emerging therapies are already available”, replied Dr. Wilens.” These include the extended-release treatments, particularly stimulants, which may reduce misuse and diversion partly because of the lack of ability to easily inject or to use these compounds intranasally.”<sup>31</sup> “Prodrugs of amphetamine are under development. One of these is a lysine-dexamphetamine compound that by nature of the covalent binding of lysine to amphetamine does not achieve significant serum levels with intranasal or intravenous abuse, and because of a complex reaction that occurs in the GI tract, obviates the rapid upswing in blood and brain levels that you might see with standard amphetamine or methylphenidate. These characteristics of the drug may translate into less euphoria. Less euphoria with any new compound will certainly reduce the abuse liability of those medications. Thus, these types of compounds should be helpful in terms of reducing the risk of abuse or even recreational misuse.”

Dr. Dodson also described a methylphenidate transdermal system that is already available. “The advantages of the transdermal system are that 1) you can actually see the patch on the person’s skin, which easily verifies compliance, and 2) once the patch is peeled off, it cannot be reattached and thus, cannot

be transferred to another person.” Although the abuse potential with transdermal systems is limited by the delivery system, reports of extraction of active drug from other transdermal products, such as fentanyl patches, has been observed. Therefore, transdermal systems do not completely limit the abuse potential.

## Stimulant Medication Therapy and Long-Term Risk of SUD

“How compelling are results of recent studies in evaluating the potential for stimulant medication therapy to reduce the likelihood of substance abuse disorder later in life?”, asked Dr. Salgo. Dr. Dodson referred to “a very good meta-analysis of data from 6 studies performed by Wilens et al in 2003<sup>6</sup> that revealed that stimulant therapy for ADHD reduced the risk of substance use disorder later in life. The real risk is in non-treatment of ADHD; untreated ADHD is associated with up to a 4-fold higher rate of SUD, compared to controls.”<sup>29</sup>

“You have to treat the ADHD, suppress the ADHD symptoms and in association, achieve improvement in the individual’s functional capacity in order to reduce the risk for substance abuse,” said Dr Wilens. “I think we’ve answered

the question: Does early stimulant treatment lead to increased risk for substance abuse? The answer is no. Does it reduce the risk for substance abuse? The answer is probably. What’s the mechanism of that risk reduction? We are currently investigating that issue.”

## Final Thoughts

“How does a clinician integrate this information in the treatment of ADHD?”, asked Dr. Salgo. “Clinicians integrate this information by educating families and patients about the potential for abuse, misuse, and diversion of stimulant medications, and encouraging vigilance in this regard,” replied Dr. Biederman. “The combination of a good alliance with the patient, education, and alertness could provide a safe environment to treat people with ADHD in the context of abuse/misuse/diversion potential.”

“Clinicians need to be educated about identifying ADHD, in terms of both presentation of ADHD symptoms and comorbid psychiatric illnesses,” added Dr. Goodman. “The order of priority is to treat alcohol and substance abuse, stabilize bipolar and mood disorders, treat anxiety disorders, and then treat ADHD.”

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# Abuse, Diversion, & Misuse of ADHD Medications

## CME TEST

**1. What percent of adults with ADHD have a prior history of substance use disorder?**

- a. 5–10%
- b. 20–30%
- c. 20–40%
- d. 2–3%

**2. What is the relative abuse potential of methylphenidate versus amphetamine?**

- a. Lower than amphetamine
- b. Same
- c. Higher

**3. How does formulating a CNS stimulant drug in a long-acting preparation impact abuse liability?**

- a. Decreases abuse potential
- b. Makes no difference
- c. Decreases diversion, but not abuse

**4. What are the most prominent psychiatric comorbid risk factors for increased abuse potential of ADHD medications in patients with ADHD?**

- a. Conduct disorder
- b. Bipolar disorder
- c. Borderline personality disorder
- d. Both a and b

**5. Which of the following treatment approaches for a patient with a history of SUD is recommended?**

- a. You can use any treatment if SUD is in the distant past
- b. Choose a non-stimulant or extended release agent and monitor if patient has a history of SUD
- c. If the SUD is recent (within previous 3 months) treat addiction before beginning ADHD treatment
- d. All of the above

**6. What are typical characteristics of people who are likely to misuse/abuse ADHD medications?**

- a. Oppositional defiance
- b. Delinquency
- c. Conduct disorder
- d. White, male college students belonging to a fraternity
- e. All of the above

**7. Which of the following are correct regarding practical strategies for decreasing abuse liability?**

- a. Never prescribe stimulant medications
- b. Monitor use of medication
- c. Prescribe extended-release form of stimulant
- d. Both b and c

**8. What is recommended as a response when you suspect or know that your patient is misusing their ADHD medication?**

- a. Discuss the proper use of medication if the patient is misusing it
- b. In case of misuse or diversion, discuss ancillary treatments for ADHD
- c. Withhold treatment for ADHD until SUD is under control and patient is in a recovery program
- d. All of the above

**9. What is the relationship between stimulant medication therapy and SUD?**

- a. Increases risk of SUD
- b. Reduces risk of SUD later in life
- c. Does not affect risk of SUD
- d. None of the above

**10. What consequences do patients face if they fail to comply with their prescribed ADHD treatment or if they are undertreated out of fear of medication abuse?**

- a. Deterioration in social relationships
- b. Increased risk of motor vehicle accidents
- c. Deterioration in academic or work performance
- d. Increased high-risk behaviors
- e. All of the above

**11. Which drug delivery systems for CNS stimulants provide efficacy while reducing abuse liability?**

- a. Transdermal drug systems
- b. Prodrugs that are activated in the gastrointestinal tract
- c. Extended-release formulations
- d. All of the above

## CME TEST ANSWER KEY

- 1. Ans. c.** [See Introduction]: Approximately 20% to 40% of adults with ADHD have a previous history of SUD.<sup>1</sup>
- 2. Ans. b.** [See Section: Abuse Potential of CNS Stimulants] “As a class, these agents have similar abuse potential,” quotes Dr. Dodson. However, their abuse potential is low, despite the prevalence of prescriptions for these medications. “Their low abuse potential is supported by findings of 2 large in-depth surveys of college students with sample sizes of approximately 9,000<sup>9</sup> and 10,000<sup>9</sup> students, respectively. These surveys found that the 1-year rate of non-medical or illicit use of prescription stimulants was only about 4%<sup>9</sup> or 5%,<sup>9a</sup> as indicated by Dr. Dodson.
- 3. Ans. a.** [See Section: Short-Acting vs Long-Acting Stimulants: Differences in Abuse Potential] Dr. Goodman declares “The greatest abuse is likely to occur with agents with short durations of action, the reason being that they can be crushed, and the powder either snorted or dissolved in water and injected intravenously.” These latter routes of drug intake result in rapid delivery to the brain and rapid onset of action/euphoria.<sup>11,12,13</sup> “The long-acting medications have less abuse potential because they are not as amenable to being crushed and snorted,”<sup>14</sup> said Dr. Biederman. In one study, only short-acting formulations were misused or diverted.<sup>16</sup>
- 4. Ans. d.** [See Section: Comorbid Psychiatric Risk Factors for Abuse Liability in Patients with ADHD] “It is well known that individuals with ADHD who also have other co-occurring problems are at higher risk for substance use disorders,” responded Dr Wilens. “In particular, patients who have ADHD plus conduct disorder or bipolar disorder are at increased risk for substance use disorders.”<sup>17</sup>
- 5. Ans. d.** [See Section: Treatment Decisions in Patients with History of SUD] As stated by Dr. Wilens “It’s critical to ascertain the patient’s past substance use history... what is the proximity of that problem to the present situation? For example, is it something that occurred ten or 15 years ago and you’re now treating somebody who is relatively free of any type of SUD history in the last 10 years? For an individual fitting this scenario, you can choose any treatment for ADHD without a lot of concern for addiction. In contrast, an individual with a relatively recent SUD history, eg, within the previous 3 months, must be assessed carefully. Is this person truly stable with their substance use? If so, I’m going to use a non-stimulant class agent like atomoxetine or bupropion. If I decide to use a stimulant, I’m definitely going to monitor the patient carefully for proper use and diversion and I’m going to prescribe one of the extended-release formulations of either methylphenidate or amphetamine. For an individual with current, active substance use history, eg, alcohol or drug abuse, the first step is aggressive treatment of the addiction followed by treatment of the underlying ADHD in rapid succession, in part to help keep that individual involved in their addiction treatment. In this individual, a non-stimulant agent should definitely be used initially. If non-stimulant treatment is not successful or cannot be used, a stimulant can be used, but only the extended-release formulation.”
- 6. Ans. e.** [See Section: Decreasing Abuse Liability] “People who are going to misuse ADHD medications are usually identifiable. They are not your average ADHD patient,” declared Dr. Dodson. Dr. Dodson and Dr. Wilens characterized people at risk for abusing or misusing ADHD medications as those with “oppositional defiance, delinquency or conduct disorder, established substance use disorder, history of misusing other types of compounds, including other prescription medications, or tendency to experiment with cocaine and other substances.”<sup>18,14,22,23</sup> “Studies looking at college students also identified white male members of a fraternity as a risk group for illicit use and diversion of prescription stimulants,” as indicated by Dr. Dodson.
- 7. Ans. d.** [See Section: Decreasing Abuse Liability] Dr. Wilens remarked that “Clinicians can stay on top of the abuse, misuse or diversion of medications by first talking about it with patients, parents, and teachers, and stating up front that they are conscious of issues around the proper use, storage, and administration of the medication. For high risk patients, I make it clear to them that I’m only going to issue monthly prescriptions of the medication and I’m going to carefully monitor pill counts. If they request medication at an increased frequency beyond what I expect based on their daily dose, then I’ll call it into question and have them come back to talk about proper use of the medicine. Other things that can be done are: to advise patients/parents to keep the medications safely stored in drawers rather than medicine cabinets, which is where people typically look for substances of abuse; rotate storage location and not publicize the fact that they are on stimulant medications; and ensure that the individual is taking the medication as prescribed. Individuals should also be made to understand that if they’re having difficulties during certain periods of the day, they need to discuss with you the appropriate dose titration; they are not to make these decisions on their own. Otherwise they may escalate the dose to the point where it’s at a very high dose and puts them at risk for misuse.” Dr. Goodman declared “Another strategy to decrease abuse liability is to use forms of medications that we think are being less misused and diverted, such as the extended-release form of stimulants as opposed to the immediate-release form.”
- 8. Ans. d.** [See Section: Responding to Apparent Abuse, Diversion, or Misuse] “I discuss with the individual the concerns of proper use of the medication and ask point blank if he or she is using the medications exactly as indicated. If not, a discussion follows. If I have a stronger indication that, in fact, they may be misusing or diverting the medication, then I often talk to them about ancillary treatments for ADHD, and about the ramifications of misusing or diverting medication, such as being expelled from university and/or being jailed for drug trafficking. By using extended-release as opposed to immediate-release treatment forms, we can reduce this as a college problem,” according to Dr. Wilens “Treatment for ADHD will have to stop and the patient will need to be treated for diversion, abuse, or misuse of the medication,” declared Dr. Biederman.
- 9. Ans. b.** [See Section: Stimulant Medication Therapy and Long-Term Risk of SUD] “A very good meta-analysis of data from 6 studies performed by Wilens et al in 2003<sup>6</sup> that revealed that stimulant therapy for ADHD reduced the risk of substance use disorder later in life,” quoted Dr. Dodson. You have to treat the ADHD, suppress the ADHD symptoms and in association, achieve improvement in the individual’s functional capacity in order to reduce the risk for substance abuse,” said Dr Wilens. “I think we’ve answered the question: Does early stimulant treatment lead to increased risk for substance abuse? The answer is no. Does it reduce the risk for substance abuse? The answer is probably.
- 10. Ans. e.** [See Section: Consequences of Not Treating ADHD] “Untreated ADHD has a negative impact on individual’s lives, both quantitatively and qualitatively. It brings with it a whole host of difficulties ranging from academic underachievement, occupational underachievement, difficulties with social relationships, increased utilization of healthcare systems, motor vehicle accidents, high-risk behaviors, and unwanted pregnancies”, replied Dr. Wilens.<sup>25,26</sup> Dr Dodson added that “People with untreated ADHD are far more likely to drop out of school, have poor work performance and employment records, have failed relationships, be involved in injury-producing motor vehicle accidents, and contract a sexually transmitted disease.”<sup>26</sup> “ADHD is not a benign condition and it impairs everything in life and has ramifications throughout life.”
- 11. Ans. d** [See Section: Emerging Therapies and Abuse Potential] “Some of the emerging therapies are already available”, replied Dr. Wilens. “These include the extended-release treatments, particularly stimulants, which seem to reduce misuse and diversion partly because of the lack of ability to easily inject or to use these compounds intranasally.” “Prodrugs of amphetamine are under development. One of these is a lysine-dexamphetamine compound that by nature of the covalent binding of lysine to amphetamine does not allow intranasal or intravenous abuse, and because of a complex reaction that occurs in the GI tract obviates the rapid upswing that you might see with just plain amphetamine or methylphenidate. These characteristics of the drug may translate into less euphoria. Less euphoria with any new compound will certainly reduce the abuse liability of those medications. Thus, these types of compounds should be helpful in terms of reducing the risk of abuse or even recreational misuse.”

Dr. Dodson also described a methylphenidate transdermal system that is already available. “The advantages of the transdermal system is that 1) you can actually see the patch on the person’s skin, which easily verifies compliance, and 2) once the patch is peeled off, it cannot be reattached and thus, cannot be transferred to another person.”

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