

# Adult ADHD: Issues and Answers

CME Newsletter of the Adult ADHD Program,  
Department of Psychiatry, NYU School of Medicine

## A 5-Point Plan for Diagnosing and Treating Adult ADHD

Clinicians increasingly face the challenge of diagnosing attention-deficit/hyperactivity disorder (ADHD) in their adult patients. Why is it a challenge? First, ADHD in adults is an emerging condition that, until relatively recently, was thought to subside as one reached adulthood. Second, the adult with ADHD may have had the condition since childhood and learned to adapt to and cope with the symptoms via substance abuse, isolation, and/or enabling partners and family members. Third, the diagnosis of this disorder is complicated by the fact that the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* criteria for ADHD were developed for children and adolescents and, therefore, need to be interpreted for the adult presentation. Fourth, the relationship between self-rated symptoms of ADHD and reports of symptom severity provided by parents, partners, and siblings remains tentative, as does the relationship between childhood and adult symptoms of ADHD. Thus, the clinician must proceed with skillful caution to correctly diagnose an adult patient with ADHD, as well as any other psychiatric comorbidities that may be present.

A way to approach such a patient is to use a 5-point plan that will methodically lead from the moment a patient walks into the office all the way to strategizing the treatment and following up on its success.

### Step 1: Get a thorough medical and psychiatric history

History speaks volumes. A systematic clinical interview is the basis of an ADHD diagnosis in adults.<sup>1</sup> Such a dialogue lets the practitioner evaluate symptoms reaching back to childhood and assess whether the patient meets the *DSM-IV* diagnostic criteria. A thorough childhood history is important for 3 reasons: (1) the amount of impairment that childhood symptoms caused could establish a pattern in terms of frequency, pervasiveness, and severity; (2) symptoms may have been overlooked or been written off as something else when the patient was a child; and (3) the patient may not have been given a diagnosis of ADHD as a child because the symptoms only surfaced with the stresses and demands of adulthood. Especially for highly functioning individuals, for whom the structured environment of elementary school may have served to suppress symptoms, the more rigorous, academically demanding, and less structured setting of college life may precipitate the emergence of symptoms. The problems that adults with ADHD typically present with include mood symptoms, lack of organization, inattentiveness, and forgetfulness. Many of the childhood symptoms of ADHD take on a different form in adulthood and do not always directly correspond with the *DSM-IV* symptoms applied to children [Table 1]. Adults have symptoms that permeate every aspect

of their lives. For example, adults with ADHD admit to road rage and aggressive driving<sup>2</sup> and are more likely to be ticketed for reckless driving, driving without a license, hit-and-run crashes, and to have their licenses suspended or revoked than non-ADHD adults.<sup>3</sup> Adult ADHD is also associated with damaged personal and spousal marriages and family tension.<sup>4</sup> Often, adults with ADHD have job-related difficulties, conflicts with authority, difficulty finding and keeping jobs, and poor work performance ratings.<sup>1,5</sup> Thus, the pivotal questions to ask may include the number of jobs the patient has had in the last 5–10 years, the reasons for losing/switching jobs, the relationship with one's boss, the number of driving infractions and the existence of a criminal record, and tension and unhappiness in relationships and family life.

### Step 2: Use rating scales

For ADHD, the Adult ADHD Clinical Diagnostic Scale v. 1.2 (ACDS) and the Conners' Adult ADHD Diagnostic Interview can aid in diagnostic evaluations. The Adult ADHD Investigator Symptom Rating

**Table 1. Symptoms of Adult and Childhood ADHD Can Differ<sup>1</sup>**

Symptoms	Children*	Adults
Inattention	Cannot organize Loses things Does not listen Forgetful Cannot complete tasks Cannot pay attention Is easily distracted	Cannot pay attention to reading/paperwork Has poor concentration Is easily distracted Forgetful Manages time poorly Misplaces things Has difficulty finishing tasks
Hyperactivity	Cannot play/work quietly On the go all the time Runs/climbs excessively Squirms and fidgets Talks excessively	Feels overwhelmed Fidgets when seated Self-selects active jobs Shows inner restlessness Talks excessively
Impulsivity	Blurts out answers Impatient; cannot wait his/her turn Intrudes on/interrupts others	Drives too fast, has traffic accidents Impulsively changes jobs Is irritable/quick to get angry

\*Symptoms as defined by *DSM-IV*.

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## Statement of Need

Attention-deficit/hyperactivity disorder (ADHD), although commonly thought of as a pediatric problem, often persists into adulthood. Efforts to make a diagnosis of ADHD in an adult are often confounded by comorbid conditions, such as bipolar, depressive, anxiety, substance use, and other personality disorders. The prevalence of comorbidity may exceed more than half of all adult patients, and symptoms, including substance abuse, impulsivity, and mood swings can, to varying degrees be attributed to any one of many psychiatric problems. To diagnose adult ADHD, practitioners need to gather a complete, detailed, longitudinal personal history of the patient, both medical and psychiatric. While episodic symptoms support the existence of mood or personality disorders, the behavioral and emotional manifestations of ADHD in adulthood may assume a seemingly unique entity. In addition to comorbidity, medical causes, such as hyperthyroidism or neurological disorders, must also be considered. Once a diagnosis of ADHD is established, careful consideration must be given to the treatment of such comorbid conditions. The primary focus of this newsletter is to provide a step-by-step algorithm for diagnosing and initiating treatment for the suspected adult ADHD patient. In addition to providing a focused perspective on adult ADHD, the newsletter also discusses recent research into commonly prescribed ADHD medications, as well as issues pertinent to the adult ADHD patient.

1. Adler L, Cohen J. Diagnosis and evaluation of adults with attention-deficit/hyperactivity disorder. *Psychiatr Clin North Am.* 2004;27:187-201.
2. 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.
3. Spencer TJ, Biederman J, Mick E. Attention-deficit/hyperactivity disorder: diagnosis, lifespan, comorbidities, and neurobiology. *Ambul Pediatr.* 2007;7(1(Suppl)):73-81.
4. Donnelly CL, Reimherr FW, Young JL. Differential diagnosis and treatment of adult ADHD and neighboring disorders. *CNS Spectr.* 2006;11(10 Suppl 11):1-14.
5. Philipsen A. Differential diagnosis and comorbidity of attention-deficit/hyperactivity disorder (ADHD) and borderline personality disorder (BPD) in adults. *Eur Arch Psychiatry Clin Neurosci.* 2006;256(Suppl 1):42-46.

## Learning Objectives

After completing this activity, you should be able to:

- Articulate a 5-point plan for diagnosing and treating ADHD
- Identify similarities and differences between the childhood and adult presentations of ADHD
- Discuss dosing, side effects, and alternative uses of commonly prescribed ADHD medications
- Identify specific manifestations of adult ADHD and medications of potential use in managing them

## Method of Participation

Read this newsletter, complete the CME Posttest Answer Form and Activity Evaluation Form, and fax or mail the forms to Medical Education Resources, Inc. at the address listed. You will receive a certificate by fax or mail. There is no certificate processing fee.

## Intended Audience

This activity was developed for psychiatrists, primary care physicians/internists, neurologists, and psychologists.

## Effective Dates

Released: September 2007  
Expires: August 31, 2008

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This activity is jointly sponsored by Medical Education Resources, Inc. and MedLearning Inc. The activity is supported by an unrestricted educational grant from Shire.

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## Unlabeled Use Disclosure Statement

Participants are advised that this CME activity will contain references to unlabeled/unapproved/investigational uses of drugs to treat ADHD.

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Scale (AISRS), The Conners' Adult ADHD Rating Scale-Observer: Screen Version (CAARS-O:SV), and the Attention-Deficit Hyperactivity Disorder Rating Scale (ADHD-RS) are useful for tracking symptoms and treatment progress. The advantage of using the ACDS or AISRS is that they include modular probes and prompts that are geared toward helping the clinician adequately establish the scope and degree of impairment of adult ADHD symptomatology. Self-report symptom scales include the Adult ADHD Self-Report Scale (ASRS), the Conners' Adult ADHD Rating Scale-Self: Short (CAARS-S:S), and the Brown ADD Scale (BAADS). While more scales exist, the important point is to select a scale that you like and are comfortable using for the majority of your patients.

## Step 3: Consider comorbidities

The patient also must be evaluated for comorbidities, as bipolar, substance use, depressive, anxiety, and personality disorders can intermingle in the ADHD patient's life, making diagnosis a challenge. One study showed that 70% of adults with ADHD had concomitant psychiatric disorders compared with 15% of adult controls, demonstrating the high prevalence of comorbidities in adult ADHD.<sup>6</sup> Evaluation and treatment of ADHD and comorbid psychiatric disorders should be part of a plan in which consideration is given to all aspects of the patient's life.<sup>7</sup> Any therapeutic intervention should follow a careful evaluation of the patient, including psychiatric, addiction, social, cognitive, educational, and family evaluations. A thorough history of substance use should be obtained, including past and current usage and treatments. Careful attention should be paid to the differential diagnoses, including medical and neurological conditions whose symptoms may overlap with ADHD (hyperthyroidism, seizure history) or may be a result of substance use disorder (SUD) (ie, protracted withdrawal, intoxication, or hyperactivity). Current psychiatric factors that contribute to the clinical presentation (symptoms of depression, anxiety, explosive behavior) need to be explored thoroughly. Keep in mind that ADHD symptoms are generally life-long, while mood disorders tend to be episodic and SUD typically has a time of onset, highlighting the importance of obtaining a longitudinal history.

## Step 4: Treat accordingly

Medications tend to play a prominent role in most treatment plans given their robust efficacy. Monotherapy with a single drug can be used first, with psychotherapy or other forms of therapy added as needed. The Food and Drug Administration (FDA) has approved for adult ADHD the second-generation long-acting stimulants mixed amphetamine salts (MAS)-extended release (XR) (Adderall XR, Shire US, Inc.)<sup>8</sup> and dexamethylphenidate (*d*-MPH) XR (Focalin XR, Novartis Pharmaceuticals),<sup>9</sup> and the nonstimulant atomoxetine (Strattera, Eli Lilly and Co.)<sup>10</sup> [Table 2]. Emerging therapies being evaluated within the adult ADHD population but not yet approved for adults include lisdexamfetamine mesylate (Vyvanse, Shire US, Inc.), which is a prodrug of dextroamphetamine,<sup>11</sup> and nonstimulant extended-release guanfacine.<sup>12</sup> Some patients report reduction of ADHD symptoms during behaviorally oriented therapies. A significant controlled trial to date of psychotherapy for ADHD found that cognitive behavioral therapy (CBT) was associated with reduction of residual ADHD symptoms in patients managed on medication.<sup>13</sup> In that study, those in the CBT group had lower rates of investigator-rated depression ( $P<0.01$ ), and a trend to lower rates of self-reported depression ( $P=0.06$ ). CBT continued to show superiority over continued psychopharmacology alone when statistically controlling levels of depression in analyses of core ADHD symptoms. Significantly more treatment responders were counted among patients who received CBT (56%) than those who did not (13%;  $P<0.02$ ). These data support the hypothesis that CBT for adults with ADHD with residual symptoms is a feasible, acceptable, and potentially efficacious next-step treatment approach, worthy of further testing.

**Table 2. Summary of FDA-Approved Medications for Adults With ADHD**

Medication	Starting Dose (Maximum Dose)	Common Adverse Events	Contraindications
Mixed amphetamine salts XR <sup>9</sup>	10 mg/day (20 mg/day)	Dry mouth, loss of appetite, insomnia, weight loss, headache, nausea, anxiety, agitation, dizziness, tachycardia, diarrhea	Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, hypersensitivity to sympathomimetic amines, glaucoma, agitation, history of drug abuse  Black box warning: high potential for abuse; misuse of amphetamines may cause sudden death and serious cardiovascular adverse events
Atomoxetine <sup>10</sup>	40 mg/day <sup>a</sup> increase to 80 mg/day after 3 days (100 mg/day)	Constipation, dry mouth, nausea, decreased appetite, dizziness, insomnia, decreased libido, ejaculatory problems, impotence, urinary problems, dysmenorrhea	Hypersensitivity to atomoxetine, narrow angle glaucoma  Black box warning: suicidal ideation in children and adolescents; not approved for major depressive disorder
Dexmethylphenidate XR <sup>9</sup>	10 mg/day (20 mg/day)	Headache, dry mouth, anxiety, dyspepsia, pharyngolaryngeal pain, feeling jittery, dizziness	Agitation, hypersensitivity to methylphenidate, glaucoma, tics

<sup>a</sup> Many clinicians start with a low dose and titrate slowly.<sup>14</sup>

**Step 5: Follow up closely**

Gauge any improvements or erosions of behavior and adjust medications accordingly, if necessary. Repeat symptom rating scales regularly. Clinical trials define improvement as ≥30% reduction in symptoms, which could be quantified using rating scales. Also, monitor whether the patient is experiencing any adverse reactions to the medications. Common side effects are shown in **Table 2**. Prompting patients to the possibility of side effects when the prescription is given will aid greatly in patients reporting intolerant reactions, in which case the dose or the drug may be changed.

**References**

- Adler L, Cohen J. Diagnosis and evaluation of adults with attention-deficit/hyperactivity disorder. *Psychiatr Clin North Am.* 2004;27:187-201.
- Richards TL, Deffenbacher JL, Rosen LA, Barkley RA, Rodricks T. Driving anger and driving behavior in adults with ADHD. *J Atten Disord.* 2006;10:54-64.
- Fischer M, Barkley RA, Smallish L, Fletcher K. Hyperactive children as young adults: driving abilities, safe driving behavior, and adverse driving outcomes. *Accid Anal Prev.* 2007;39:94-105.
- Eakin L, Minde K, Hechtman L, et al. The marital and family functioning of adults with ADHD and their spouses. *J Atten Disord.* 2004;8:1-10.
- Barkley RA, Fischer M, Smallish L, Fletcher K. The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. *J Abnorm Psychol.* 2002;111:279-289.
- Minde K, Eakin L, Hechtman L, et al. The psychosocial functioning of children and spouses of adults with ADHD. *J Child Psychol Psychiatry.* 2003;44:637-646.
- 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.
- Adderall XR [prescribing information]. Wayne, PA: Shire US Inc; 2007.
- Focalin XR [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Inc; 2007.
- Strattera [prescribing information]. Indianapolis, IN: Eli Lilly and Company; 2007.

- Jasinski D, Krishnan S. A double-blind, randomized, placebo and active controlled, 6 period crossover study to evaluate the likability, safety, and abuse potential of lisdexamfetamine dimesylate (LDX) in adult stimulant abusers [abstract 236]. Program and abstracts of the 19th U.S. Psychiatric & Mental Health Congress; November 15-19, 2006; New Orleans, Louisiana.
- Swearingen D, Pennick M, Shojaei AH, Fiske K, Robinson J, Scheckner B. Pharmacokinetic analysis of guanfacine extended release in healthy adults [abstract 233]. Program and abstracts of the 19th U.S. Psychiatric & Mental Health Congress; November 15-19, 2006; New Orleans, Louisiana.
- Safren SA, Otto MW, Sprich S, et al. Cognitive-behavioral therapy for ADHD in medication-treated adults with continued symptoms. *Behav Res Ther.* 2005;43: 831-842.
- Adler LA. Adult Presentations of Childhood Disorders, Presented at the Annual Meeting of the Academy of Child and Adolescent Psychiatry, Washington DC, October, 2004.

**Atomoxetine Can Raise BP in Patients with Autonomic Dysfunction**

Critical disruptions or imbalances of autonomic function can result from spinal cord injury and diabetes. New research shows that the nonstimulant atomoxetine used in treating ADHD can cause elevated blood pressure in individuals with impaired autonomic function.<sup>1</sup> Atomoxetine, which is considered a selective norepinephrine transporter blocker, has the potential to cause hypertension by boosting the concentration of norepinephrine in peripheral sympathetic neurons. This effect may be masked in healthy subjects by central sympathetic mechanisms. In a study that tested this theory, the pressor effect of atomoxetine 18 mg (the pediatric dose) was evaluated in 21 patients with damage to the central and peripheral autonomic nervous system. Atomoxetine was administered in a randomized, crossover, placebo-controlled fashion, and blood pressure and heart rate were measured at baseline and for 1 hour following drug administration. Atomoxetine acutely increased seated and standing systolic blood pressure (SBP) in patients with central autonomic failure by a respective mean of 54 ( $P=0.004$ ) and 45 mm Hg ( $P<0.02$ ), respectively, compared with placebo. At the end of the observation period, the mean seated SBP in the atomoxetine group was in the hypertensive range (149 mm Hg; range 113-209 mm Hg). However, in patients with peripheral

autonomic failure, atomoxetine did not elicit a pressor response; seated and standing SBP increased by 4 mm Hg ( $P=0.7$ ) and 0.6 mm Hg ( $P=0.5$ ) with atomoxetine, compared with placebo. Thus, atomoxetine induces a notable blood pressure increase in patients with central autonomic failure even at very low doses. These results imply that a functional central sympatholytic pathway is essential to avoid hypertension in patients treated with this agent. Atomoxetine is generally well tolerated with mild blood pressure elevations in most individuals. The clinical trials in normotensive individuals found an average change of 2-3 mm Hg in systolic and diastolic blood pressure.<sup>2</sup> Therefore, exercise caution when prescribing atomoxetine in patients with a history of autonomic instability.

## References

1. Shibao C, Raj SR, Gamboa A, et al. Norepinephrine transporter blockade with atomoxetine induces hypertension in patients with impaired autonomic function. *Hypertension*. 2007;50(1):47-53. Epub ahead of print May 21.
2. Michelson D, Adler L, Spencer T, et al. Atomoxetine in adults with ADHD: two randomized, placebo-controlled studies. *Biol Psychiatry*. 2003;53:112-120.

## Amphetamine dependence may be treatable

Stimulant medications are highly effective and generally well-tolerated treatments for adult ADHD. However, abuse of stimulants can have some serious medical consequences. Amphetamine abuse, for example, can be deadly. A recent study showed that amphetamine abuse may significantly increase the rate of hospital admissions for strokes and stroke-related mortality.<sup>1</sup> A cross-sectional analysis of a Texas hospital database that included over 3 million patients, 18-44 years old, showed that amphetamines were abused more frequently than cocaine and cannabis. To that end, the stroke rate also increased among amphetamine abusers. In more than 800,000 discharges that were assessed, amphetamine abusers had a 5-fold increase in hemorrhagic stroke, twice that of those who abused cocaine. In addition, amphetamine, but not cocaine, abuse was associated with a 2.6-fold increase in risk of death after hemorrhagic stroke. Unfortunately, no pharmacotherapy has proven effective for amphetamine dependence. Another recent study compared methylphenidate, aripiprazole, and placebo in patients with amphetamine dependence.<sup>2</sup> In this study, 53 people who met *DSM-IV* criteria for amphetamine dependence were randomly assigned to receive the antipsychotic drug aripiprazole (15 mg/day), slow-release methylphenidate (54 mg/day), or placebo for 20 weeks. The study was terminated prematurely due to unexpected results of interim analysis. An intention-to-treat analysis was used. The primary outcome measure was the proportion of amphetamine-positive urine samples. The results showed that patients allocated to aripiprazole had significantly more amphetamine-positive urine samples than patients in the placebo group (odds ratio=3.77), whereas patients who received methylphenidate had significantly fewer amphetamine-positive urine samples than patients who had received placebo (odds ratio=0.46). Based on these findings, methylphenidate may be an effective treatment for reducing severe amphetamine dependence.

## References

1. Westover AN, McBride S, Haley RW. Stroke in young adults who abuse amphetamines or cocaine: a population-based study of hospitalized patients. *Arch Gen Psychiatry*. 2007;64:495-502.
2. Tiihonen J, Kuoppasalmi K, Fohr J, et al. A comparison of aripiprazole, methylphenidate, and placebo for amphetamine dependence. *Am J Psychiatry*. 2007;164:160-162.

## A lawyer with ADHD masked by depression

Jeff is a 48-year-old attorney, graduate of a top 10 law school, and now a litigator in a large NYC law firm. He experiences trouble at work in terms of managing multiple meetings, but his demeanor in court is legendary. Jeff is married and has chronic conflicts regarding him "listening" to his wife. He smokes cigarettes, which help keep him calm. He presents with vegetative symptoms of depression including guilty ruminations, somatic preoccupation, early and middle insomnia, difficulties in concentrating, decreased libido, and anoxia. Family history is significant for major depression in a parent.

Jeff's mental status examination is notable for depressed mood and constricted affect. He has been found to have ruminative thoughts. There are no psychotic symptoms, and no suicidal or homicidal ideation.

Over the last 5 years, Jeff has been treated for major depression with a variety of medications, including SSRIs (fluoxetine, paroxetine, sertraline) without response for depression. He had a modest response to venlafaxine and bupropion. All of these trials were with adequate doses and of proper duration. An attempt to augment citalopram 60 mg/day with methylphenidate to treat refractory depression led not only to improvement in depression, but also to improvement in his ability to multitask at work and listen to his wife. He also has been able to stop smoking.

With the lifting of his depression, he is now able to provide a more accurate picture of his childhood. He acknowledges that he was messy and often lost things. He left everything for the last minute, but was able to pull things out to meet deadlines. He started drinking coffee at an early age, as it helped him concentrate and get his work done. Prior to methylphenidate, he acknowledged trouble with task initiation and completion, easy distraction, trouble listening to others, and misplacing items. On citalopram 60 mg/day and sustained-release methylphenidate 40 mg/day, his work performance has vastly improved and his marriage is on much sounder ground.

*Take-home point:* Look for ADHD in patients with major depression or other mood disorders. The patient had such a serious depression that his ruminative thoughts in part clouded his retrospective recall of childhood symptoms and limited the ability to make a diagnosis of inattentive ADHD, until the depression lifted somewhat. Also, treating the most impairing disorder first, in this case the major depression, is vital to the success of treating his ADHD.

## Journal reviews

### MPH/ATX may enhance histamine, a key ingredient to alertness

The effects of histamine on cognition and alertness have been well established.<sup>1</sup> H3 receptor blockade, able to elevate concentrations of histamine, acetylcholine, dopamine, serotonin, noradrenaline, and glutamate, may offer a means for targeting cognitive processes, which often rely on the integration of multiple neurotransmitter systems.<sup>2</sup> This has sparked interest in the potential use of histamine H3 receptor antagonists for the treatment of ADHD. Blockade of histamine H3 autoreceptors increases histamine release and has been shown to improve cognitive function in animal models.<sup>3</sup> While the dopaminergic mechanisms that can activate histamine have been identified, whether certain molecules can indirectly increase histamine release is a matter still being researched. A preclinical study has shown that 2 key agents for treating adult ADHD, methylphenidate (MPH) and atomoxetine (ATX), may increase histamine release in the prefrontal cortex of the rat.<sup>3</sup> In this study, the effects of MPH 1 mg/kg SC, ATX 1 mg/kg SC,

and vehicle on histamine release were observed. Methylphenidate and atomoxetine had a significant overall treatment effect ( $P<0.001$ ) and drug-induced histamine increases were significantly different from vehicle starting at 45 minutes (MPH) and 60 minutes (ATX) after dosing. The effects of the 2 drugs were not significantly different from each other ( $P=0.6$ ). Since MPH and ATX have no substantial affinity for histamine H3 receptors, the histamine increase produced by both agents is probably a secondary effect, perhaps mediated by the enhanced cortical dopamine and/or norepinephrine levels. Improvements in cognition and attention that follow central activation of noradrenergic and the dopaminergic systems by ADHD drugs may result from cortical  $\alpha 2A$ -adrenoceptor and dopamine D1-receptor stimulation. While the clinical response to ADHD drugs has been traditionally attributed to the modulation of norepinephrine and dopamine, these results imply that enhanced histamine release may contribute to their efficacy as treatments for ADHD. Further studies are needed to show a relationship between the doses used in this preclinical study and clinically relevant drug levels must be determined before concluding that histamine plays a major role in the effects of these drugs.

### Alcohol abuse comorbid with ADHD may occur in teen years

The National Comorbidity Survey Replication demonstrated that adult ADHD is significantly comorbid with SUD, and, in fact, persons with ADHD are 3 times more likely to experience alcohol and/or drug dependence than their non-ADHD peers.<sup>4</sup> How early in life does such behavior emerge? A study by Molina and colleagues at the University of Pittsburgh assessed age specificity in the risk for heavy drinking and alcohol use disorder among 364 adolescents and young adults with ADHD diagnosed in childhood.<sup>5</sup> These individuals were compared with demographically age-matched adolescents and adults. The results showed alcohol intake started at approximately age 15, with 15- to 17-year-olds reporting being intoxicated on alcohol 14 times the previous month vs less than twice for their non-ADHD peers. Also, 14% of those with ADHD were diagnosed with alcohol abuse or dependence vs 0% of the non-ADHD group. Also, 42% of those children with ADHD who also had serious, persistent behavior problems later had alcohol abuse or dependence by ages 18 to 25. Such dependence erodes social relationships and success in school and at work. Interestingly, the tendency for teens to drink is linked to the amount of alcohol in their homes. Parents of a child with untreated ADHD may lack the proper parenting skills to handle the stresses of having a child with ADHD and may turn to alcohol as a coping mechanism. This may, in turn, begin a similar cycle for the child with ADHD. While not all children who have ADHD will become alcoholics, children should be monitored for substance abuse and treated for ADHD as they enter early adulthood.

### Nicotine patches may improve mood in adults with ADHD

Tobacco smoking is a major cause of preventable diseases, including cardiovascular disease. Adults with ADHD or with a childhood history of ADHD have higher smoking prevalence and lower cessation rates than the general population, but the causes are not well understood.<sup>6,7</sup> A study presented at the 2007 Society of Biological Psychiatry Annual Meeting examined the impact of nicotine on symptoms, moods, and cardiovascular activity in both smokers and nonsmokers with ADHD.<sup>8</sup> Here, 26 adults (14 smokers and 12 nonsmokers) were diagnosed with ADHD per *DSM-IV* criteria. Approximately every 30 minutes while subjects were awake, ADHD symptoms and moods were entered into an electronic diary; blood pressure was also monitored. In a

double-blind, counterbalanced, crossover design, participants had 2 days on a daily placebo patch and 2 days on a daily nicotine patch (21 mg for smokers, 7 mg for nonsmokers). Smokers were asked to abstain from smoking during experimental days. The results showed that nicotine reduced self-reported anger ( $P<0.01$ ) and increased ratings of self-control and happiness ( $P<0.05$  for both) compared with placebo. Also, nicotine boosted heart rate ( $P<0.001$ ), systolic ( $P<0.05$ ), and diastolic blood pressure ( $P<0.01$ ). No clinical differences were found between smokers and nonsmokers and, thus, these effects cannot be attributed solely to nicotine withdrawal. This study makes 3 points: (1) nicotine positively affects mood and self-control in smokers and nonsmokers with ADHD; (2) these reinforcing effects may, in part, explain the higher smoking prevalence and lower cessation rates in adults with ADHD; and (3) nicotine-induced elevations in cardiovascular activity may promote heart disease in adults with ADHD.

### References

1. Leurs R, Bakker RA, Timmerman H, De Esch IJP. The histamine H3 receptor from gene cloning to H3 receptor drugs. *Nat. Med.* 2005;4:107-120.
2. Esbenshade TA, Fox GB, Cowart MD. Histamine H3 receptor antagonists: preclinical promise for treating obesity and cognitive disorders. *Mol Interv.* 2006;6:77-88.
3. Horner WE, Johnson DE, Schmidt AW, Rollema H. Methylphenidate and atomoxetine increase histamine release in rat prefrontal cortex. *Eur J Pharmacol.* 2007;558:96-97.
4. 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.
5. Molina BS, Pelham WE, Gnagy EM, Thompson AL, Marshal MP. Attention-deficit/hyperactivity disorder risk for heavy drinking and alcohol use disorder is age specific. *Alcohol Clin Exp Res.* 2007;31:643-654.
6. Kollins SH, McClernon FJ, Fuemmeler BF. Association between smoking and attention-deficit/hyperactivity disorder symptoms in a population-based sample of young adults. *Arch Gen Psychiatry.* 2005;62:1142-1147.
7. Humfleet GL, Prochaska JJ, Mengis M, et al. Preliminary evidence of the association between the history of childhood attention-deficit/hyperactivity disorder and smoking treatment failure. *Nicotine Tob Res.* 2005;7:453-460.
8. Gehricke J, Hong N, Steinhoff K, Whalen CK, Jamner LD, Wigal TL. The mood and arousal enhancing effects of transdermal nicotine patches in the daily lives of adult smokers and nonsmokers with ADHD [abstract 126]. *Biol Psychiatry.* 2007;61:41S.

## Posttest

Please select only one answer for each question. Circle the letter corresponding to the correct answer on the answer form on the next page.

1. What symptoms of ADHD are shared by both children and adults?
  - A. Poor time management
  - B. Runs or climb incessantly
  - C. Talks excessively
  - D. Feel overwhelmed
2. Adults with ADHD are more likely than their non-ADHD peers to have problems with which of the following:
  - A. Driving
  - B. Job performance
  - C. Personal relationships
  - D. All of the above
3. Which rating scale is useful for tracking ADHD symptoms and progress?
  - A. ACDS
  - B. Conners' Adult ADHD Diagnostic Interview
  - C. AISRS
  - D. BAADS
4. Which medication has not yet been approved for adult ADHD?
  - A. Lisdexamfetamine mesylate
  - B. Mixed amphetamine salts extended release
  - C. Atomoxetine
  - D. *d*-methylphenidate
5. What is the maximal FDA-approved daily dose of mixed amphetamine salts extended release in adult ADHD?
  - A. 10 mg
  - B. 20 mg
  - C. 30 mg
  - D. 40 mg
6. Which medication has a black box warning about suicidal ideation?
  - A. Mixed amphetamine salts extended release
  - B. Atomoxetine
  - C. *d*-methylphenidate
  - D. All of the above
7. What is the maximal FDA-approved daily dose of atomoxetine in adult ADHD?
  - A. 20 mg/day
  - B. 40 mg/day
  - C. 80 mg/day
  - D. 100 mg/day
8. A cross-sectional analysis of a Texas hospital database that included over 3 million patients, 18-44 years old, showed that which drug(s) was abused more frequently than cocaine and cannabis?
  - A. Methylphenidate
  - B. Atomoxetine
  - C. Amphetamines
  - D. Benzodiazepines
9. A recent animal model study has shown that both methylphenidate and atomoxetine have the potential to increase which substance in the prefrontal cortex?
  - A. Histamine
  - B. Acetylcholine
  - C. Dopamine
  - D. Glutamate
10. A recent study on the effects of nicotine patches in adult ADHD patients showed all but which of the following to be true?
  - A. Nicotine positively affects mood and self-control in smokers and nonsmokers with ADHD
  - B. Nicotine's reinforcing effects may explain the higher smoking prevalence in adults with ADHD
  - C. Nicotine-induced elevations in cardiovascular activity may promote heart disease in adults with ADHD
  - D. ADHD patients have a higher smoking cessation rate than their non-ADHD peers

## Adult ADHD: Issues and Answers

Successful completion of the posttest examination (at least 70% correct) and activity evaluation is required to earn a maximum of .75 AMA PRA Category I Credits™. Statements of Credit will be awarded upon successful completion of the posttest and evaluation.

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### Posttest Answer Form

(Circle the correct answer to each question)

- |            |             |
|------------|-------------|
| 1. A B C D | 6. A B C D  |
| 2. A B C D | 7. A B C D  |
| 3. A B C D | 8. A B C D  |
| 4. A B C D | 9. A B C D  |
| 5. A B C D | 10. A B C D |

To receive credit, you must answer 7 of the 10 posttest questions correctly, complete all forms, and submit them by August 31, 2008.

### Registration for Credit (please print)

First Name: \_\_\_\_\_

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I certify that I have completed this CME activity. The actual amount of time I spent on this activity was \_\_\_\_ minutes.

Signature \_\_\_\_\_ Date \_\_\_\_\_

### Activity Evaluation Form

Please circle the appropriate rating in answer to the questions that follow:

- How would you rate the content of this CME activity?  
 Poor 1 2 3 4 5 Outstanding
- How relevant was the content of this activity to your practice?  
 Not relevant at all 1 2 3 4 5 Very relevant
- To what degree were you able to meet each of the learning objectives of the activity? Please respond to each learning objective listed below:
  - Articulate a 5-point plan for diagnosing and treating ADHD  
 Poor 1 2 3 4 5 Outstanding
  - Identify similarities and differences between the childhood and adult presentations of ADHD  
 Poor 1 2 3 4 5 Outstanding
  - Discuss dosing, side effects, and alternative uses of commonly prescribed ADHD medications  
 Poor 1 2 3 4 5 Outstanding
  - Identify specific manifestations of adult ADHD and medications of potential use in managing them  
 Poor 1 2 3 4 5 Outstanding
- Based on your knowledge and experiences, the level of the activity was:  
 Basic Appropriate Complex
- How would you rate the activity overall?  
 Poor 1 2 3 4 5 Outstanding
- Do you believe this activity was fair, balanced, and free of commercial bias?
  - Yes No
  - If No, please state the reason:  
 \_\_\_\_\_  
 \_\_\_\_\_
- How much did this activity enforce your current clinical opinions?  
 Not at all 1 2 3 4 5 A lot
- How much new information did you find in this activity?  
 None 1 2 3 4 5 A lot
- As a result of this activity, will you alter your practice?  
 Yes No
- If Yes, please describe any change(s) you plan to make:  
 \_\_\_\_\_  
 \_\_\_\_\_
- How committed are you to making these changes?  
 Not at all committed 1 2 3 4 5 Very committed
- If No, why not? \_\_\_\_\_
- Additional comments about this activity?  
 \_\_\_\_\_  
 \_\_\_\_\_
- Do you feel future activities on this subject matter are necessary and/or important to your practice?  
 Yes No
- Please list any other topics that would be of interest to you for future educational activities.  
 \_\_\_\_\_  
 \_\_\_\_\_




## Adult ADHD: Issues and Answers

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