ACADEMIC HIGHLIGHTS

ADHD and Comorbid Disorders in Adults

In the United States, approximately 4.4% of adults have attention-deficit/hyperactivity disorder (ADHD), and the average worldwide prevalence in adults is about 3.4%. However, in the United States, only about 1 in 10 adults with ADHD is currently treated specifically for ADHD. Adults with ADHD are likely to have adaptive impairments, evidenced by educational difficulties, a history of erratic employment, relationship and marital difficulties, credit or money problems, driving problems, risky sexual behavior, poor physical health, and substance abuse problems. Additionally, adults with ADHD commonly have comorbid disorders, such as mood and anxiety disorders or sleep problems, which may mask the symptoms of ADHD.

Dr. Barkley, Ph.D., discussed criteria for diagnosing ADHD in adults.

Diagnostic Challenges in Identifying ADHD in Adults

Dr. Barkley, Ph.D., discussed the highlights of the planning teleconference series “ADHD and Comorbid Disorders in Adults,” which was held in January and February 2008. This report was prepared by the CME Institute of Physicians Postgraduate Press, Inc., and was supported by an educational grant from Eli Lilly and Company.

The planning teleconference was chaired by Lenard A. Adler, M.D., Departments of Psychiatry, Neurology, and Child and Adolescent Psychiatry, New York University School of Medicine, New York. The faculty were Russell A. Barkley, Ph.D., Department of Psychiatry, State University of New York Upstate Medical University, Syracuse; and Jeffrey H. Newcorn, M.D., Department of Psychiatry, Mount Sinai School of Medicine, New York, N.Y.

Financial disclosure: Dr. Adler has received grant/research support from Abbott, Cortex, Bristol-Myers Squibb, Merck, Novartis, Pfizer, Shire, Eli Lilly, Ortho-McNeil/Janssen/Johnson & Johnson, New River Pharmaceuticals, Cephalon, and the National Institute on Drug Abuse; is a member of the speakers bureaus for Eli Lilly and Shire; and is a member of the advisory boards and is a consultant for Abbott, Cortex, Novartis, Pfizer, Shire, Eli Lilly, Ortho-McNeil/Janssen/Johnson & Johnson, New River Pharmaceuticals, Cephalon, Merck, Organon, Sanofi-Aventis, and Psychogenics.

Dr. Barkley is a consultant for Eli Lilly, Shire, and Abbott; has received grant/research support from the National Institute of Mental Health; has received honoraria from the Canadian Attention Deficit Hyperactivity Disorder Resource Alliance, the Campus Alcohol and Drug Education Center of California State University, the Learning Disabilities-Attention Disorder Program of North Carolina, TheaCare, the National Association of School Psychologists, the Medical College of Wisconsin, the New England Educational Institute, Egleston Children’s Hospital, Spanish Child Psychiatry Association, the Portugal ADHD Foundation, the Brazil ADHD Parents Association, the Uruguay ADHD Parents Association, and the Argentina Mental Health Conference; is a member of the speakers/advisory boards for Eli Lilly, Shire, Novartis, and Janssen; and has received other financial or material support from Guilford Publications, Compact Clinics, the New England Educational Institute, and J & K Seminars. Dr. Newcorn is an advisor/consultant for Eli Lilly, McNeil, Shire, Lupin, Sanofi-Aventis, Abbott, and Psychogenics; has received grant/research support from Eli Lilly and McNeil; and has received honoraria for speaking from Eli Lilly, Shire, and Novartis.

The opinions expressed herein are those of the faculty and do not necessarily reflect the views of the CME provider and publisher or the commercial supporter.

Problems With the Current Diagnostic Criteria for ADHD in Adults

The DSM-IV-TR criteria for ADHD were developed for diagnosing children and were not intended for use in adults. Because of differences between adult and childhood ADHD, Dr. Barkley suggested modifications in the criteria for diagnosis of ADHD in adults.

Symptom descriptions. Given that the majority of children with ADHD continue to have the disorder in adulthood, the DSM-IV-TR descriptions of ADHD symptoms need to be adjusted for adults. For example, the hyperactive and impulsive symptoms prominent in childhood become internalized with age; as adults, these individuals feel a mental restlessness and a need to be busy, although they may complete few activities. Whereas children may exhibit behavioral impulsiveness, adults are likely to show impulsive decision making and verbal impulsiveness, which produces symptoms such as excessive talking, blurting out answers, and not letting others finish speaking. Dr. Barkley added that the inattention attributed to ADHD probably represents impairment in executive functioning or the cognitive abilities that are used to regulate behavior.
The executive deficits related to inattentive symptoms become increasingly prominent and impairing by adulthood. Descriptions of symptoms in adults need to include problems with time management, working memory, risk-taking, and impulse control.

**Developmentally referenced cutoffs.** Cutoff scores need to be adjusted for adults, according to Dr. Barkley. The DSM-IV-TR threshold of 6 of 9 symptoms required for diagnosis of ADHD is too high for adults. Dr. Barkley recommended that clinicians use a threshold for adults of 4 of 9 symptoms, which can still constitute meaningful dysfunction.

**Sex-referenced rating scales.** The DSM-IV-TR criteria for ADHD were developed in a field trial comprising more boys than girls, thus weighting the criteria toward male symptomatology. Dr. Barkley suggested that clinicians employ sex-referenced rating scales, such as the Conners’ Adult ADHD Rating Scales (CAARS), that have separate norms for women and men to better assess ADHD symptoms in women.

**Age at onset.** The DSM-IV-TR diagnostic criteria for ADHD require onset of symptoms prior to 7 years of age. Dr. Barkley stated that when the criteria are revised, an age at onset prior to 16 years of age will likely be specified for adult ADHD. No precise age will be required because patient and family reports of the age at onset are often unreliable in adults.

**Developmental deviance.** The DSM-IV-TR criteria do not specify how to establish developmental inappropriateness for the symptoms of inattention and hyperactivity or impulsivity. Dr. Barkley suggested that clinicians use the 93rd percentile, or 1.5 standard deviations above the mean, on a well-normed rating scale of ADHD symptoms for adults as the indicator of developmental deviance.

**Corroboration of reports.** For a diagnosis of ADHD in adults, a requirement should be added that clinicians obtain and document corroboration of information about symptoms and impairments described by the patient. Patients under age 30 years tend to underreport the severity of symptoms and impairments in current major life activities. Conversely, overreporting of symptoms or malingering can also occur, especially in instances where some financial or legal outcome is contingent on the evaluation.

**Definition of impairment.** Dr. Barkley stressed that impairment is a requirement for the diagnosis of ADHD. The DSM-IV-TR does not define the term impairment, but according to the Americans With Disabilities Act of 1990, impairment substantially limits 1 or more major life activities. Patients should be compared with the average person in the population rather than a high-functioning peer group; the term impairment cannot be applied because an individual’s behavior and its consequences fall below expectations for the patient’s level of intelligence.

**Major life activities.** The major adult life activities of marriage, childrearing, managing money, driving, sexual activity, and social relationships need to be added to the diagnostic criteria for home, school, and work settings currently specified in DSM-IV-TR. Adults with ADHD have problems handling these daily responsibilities.

### Table 1. Proposed Criteria for ADHD in Adults

<table>
<thead>
<tr>
<th>Cutoff: Either 4 of the first 7 or 6 of 9 symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at onset:</strong> Childhood to adolescence (&lt; 16 years of age)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ADHD = attention-deficit/hyperactivity disorder, DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision, EF = executive function.

### ACADEMIC HIGHLIGHTS

The study identified 9 essential problems for adults with ADHD, retaining only a few useful symptoms from DSM-IV-TR (Table 1). These requirements form a better set of criteria for adult ADHD than current criteria, according to Dr. Barkley.

Distractibility, making impulsive decisions, and executive deficits that
affect perseverance in activities or doing things in the correct sequence are better symptoms for identifying ADHD in adults than hyperactivity. However, attention problems cut across many psychiatric disorders and may not be particularly useful for differential diagnosis. A symptom that proved to be specific to adults with ADHD was problems with driving. Adults with ADHD have been found to be especially at risk for speeding citations and automobile accidents.14

**Subtypes of ADHD.** The subtypes of ADHD (i.e., inattentive, hyperactive/impulsive, and combined) specified in the DSM-IV-TR need to be revised, said Dr. Barkley. The hyperactive form of ADHD is rare in adults; children with this type of ADHD usually move into the combined type as executive and attention deficits develop.11 Inattentive type ADHD needs to be reclassified into the following 3 groups: (1) people who have outgrown hyperactive symptoms and no longer meet all the criteria for combined type ADHD, (2) individuals who are 1 or 2 symptoms short of the 12 symptoms currently required for the combined type, and (3) a group that exhibits sluggish cognitive tempo, which comprises individuals who do not have difficulties with hyperactivity or impulse control but who appear shy or withdrawn; have problems with staring, daydreaming, passivity, or confusion; and have difficulties focusing on the important versus the unimportant.15

**Conclusion**

Dr. Barkley offered clinical guidelines for assessing adult ADHD (Table 2)5,8 and stated that adult ADHD is a valid disorder that can be diagnosed using the DSM-IV-TR criteria with some adjustments. Although impairment in major life activities begins early in life for patients with ADHD, numerous issues that are less likely to be present in the diagnosis of children apply to the assessment and diagnosis of adults.

**Managing ADHD and Comorbid Disorders**

Jeffrey H. Newcorn, M.D., stated that the relationships and boundaries between ADHD and comorbid disorders are not well defined. Accurate diagnosis is difficult because comorbidities such as anxiety and learning difficulties may be concealed by more obvious ADHD symptoms, and conversely, ADHD symptoms may be concealed by more robust symptoms of severe depressive, conduct, bipolar, or substance use disorders (SUD). However, distinguishing among these disorders is important because they inform appropriate treatment.

**Prevalence of Adult ADHD and Psychiatric Comorbidities**

Comorbidity is common in adults with ADHD. Data from the National Comorbidity Survey Replication1 showed that among 3199 respondents, adults with ADHD had substantial comorbidity with mood and anxiety disorders, SUD, and impulse control disorders within the previous 12 months (Figure 1), and adults with those disorders had substantial comorbidity with ADHD (Figure 2). However, Dr. Newcorn explained that comorbid
disorders may be a direct reflection of ADHD symptoms and their impact; for example, the experiences of doing poorly in certain academic activities such as tests in school may lead to anxiety regarding performance and low self-esteem regarding poor achievement. Some comorbid disorders, such as bipolar disorder, may actually be genetic variants of ADHD, whereas other frequently occurring comorbid conditions, such as depressive disorders, share common environmental risk factors with ADHD.

Differences in Comorbidity Across Age Groups

Comorbid disorders may differ between children and adults with ADHD. For example, a comparison of children and adults with ADHD and comorbid psychiatric disorders found that children more often have comorbid oppositional defiant disorder, but adults with ADHD more often have comorbid anxiety disorders (Table 3), although interpretation is somewhat constrained by the size of some of the comorbid groups. Other comorbid disorders that often occur in adults are major depressive disorder (MDD) and SUD. Some of the cognitive problems in ADHD are difficult to distinguish from learning disabilities, which may confuse differential diagnosis in adult patients who have a history of underachievement. Additionally, personality disorders are common among adults who had ADHD in childhood.

Table 3. Rates of Psychiatric Disorders in Groups of Subjects With ADHD and in Adult Comparison Subjects Without ADHD

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Referred Adults With ADHD (N = 84)</th>
<th>Nonreferred Adult Relatives With ADHD (N = 36)</th>
<th>Referred Children With ADHD (N = 140)</th>
<th>Comparison Adults Without ADHD (N = 207)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
</tr>
<tr>
<td>Oppositional disorder</td>
<td>24 29a,e</td>
<td>19 53d</td>
<td>92 66</td>
<td>5 2</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>17 20b</td>
<td>12 33d</td>
<td>30 21</td>
<td>8 4</td>
</tr>
<tr>
<td>Antisocial personality</td>
<td>10 12a</td>
<td>6 18b</td>
<td>...</td>
<td>6 3</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>26 31a</td>
<td>6 17a</td>
<td>40 29</td>
<td>11 5</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>21 25c</td>
<td>6 17a</td>
<td>1 0.7</td>
<td>17 8</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>23 27a,e</td>
<td>13 36e</td>
<td>2 1</td>
<td>27 13</td>
</tr>
<tr>
<td>Drug abuse</td>
<td>17 20c</td>
<td>7 19e</td>
<td>0 0</td>
<td>12 6</td>
</tr>
<tr>
<td>Drug dependence</td>
<td>15 18e</td>
<td>6 17a</td>
<td>1 0.7</td>
<td>12 6</td>
</tr>
<tr>
<td>Multiple anxiety</td>
<td>42 50d</td>
<td>15 42f</td>
<td>39 28</td>
<td>28 14</td>
</tr>
<tr>
<td>Overanxious disorder</td>
<td>43 52b,ef</td>
<td>14 40f</td>
<td>42 30</td>
<td>22 11</td>
</tr>
<tr>
<td>Separation anxiety disorder</td>
<td>6 7a</td>
<td>4 11</td>
<td>40 29</td>
<td>7 3</td>
</tr>
<tr>
<td>Generalized anxiety</td>
<td>36 43d</td>
<td>7 20d</td>
<td>...</td>
<td>10 5</td>
</tr>
<tr>
<td>disorder</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agoraphobia</td>
<td>6 7b</td>
<td>1 3</td>
<td>13 9</td>
<td>1 0.5</td>
</tr>
<tr>
<td>Social phobia</td>
<td>27 32d</td>
<td>12 33c</td>
<td>18 13</td>
<td>27 13</td>
</tr>
</tbody>
</table>

ADHD symptoms produces a corresponding change in anxiety symptoms. However, if the conditions are relatively independent and the anxiety is greatly impairing, the anxiety should be treated at the same time or even first.

Substance abuse. Adults with ADHD have elevated rates of SUD and an earlier age at onset of SUD (19.1 vs. 22.0 years of age) compared with adults without ADHD. Research has examined whether ADHD stimulant pharmacotherapy sensitizes individuals to increase the risk of using other stimulants, such as cocaine, later in life. Studies in humans suggest that this is not the case and have found either no effect of treatment on substance abuse or a decrease in risk that may result from treatment of impulsivity. The risk for substance abuse is particularly high among adolescents and young adults with ADHD, but Dr. Newcorn noted that the relationship between ADHD and early onset of substance abuse suggests that there may be a window of opportunity for treatment.

The only substance of abuse found to have a specific association with ADHD is nicotine. Nicotine impacts neural circuits in the brain that enhance attention, which may account for the specificity of risk in ADHD. Dr. Newcorn observed that nicotine may serve as a "gateway" drug for SUD, preceding the use of other substances of abuse and producing changes in neural function that increase addiction susceptibility. Nicotine use also has important psychosocial consequences. Smoking cigarettes is illegal for adolescents, and adolescents who smoke cigarettes are more likely to be exposed to peers who use other drugs or are involved in other illicit behaviors. Thus, targeting the potential for nicotine use and abuse among adolescents with ADHD is of paramount importance.

Learning disabilities. The impairments associated with ADHD can be increased by the co-occurrence of specific learning disabilities. A substantial number of children with ADHD have comorbid learning disabilities and continue to show cognitive and academic impairments in adolescence and adulthood.

ADHD and Specific Common Psychiatric Comorbidities

Mood and anxiety disorders. Dr. Newcorn advised that focusing on the developmental course of the patient's conditions can help distinguish whether mood and anxiety disorders are independent of or secondary to ADHD, which can have important implications for the sequencing of treatment. For example, if ADHD preceded an anxiety disorder, and the anxiety is specific to performance situations, the clinician might decide to treat the ADHD first and see whether improvement in ADHD symptoms produces a corresponding change in anxiety symptoms. However, if the conditions are relatively independent and the anxiety is greatly impairing, the anxiety should be treated at the same time or even first.
adulthood. The consequences of learning disabilities among individuals with ADHD include academic underachievement, grade repetition, school dropout, and working below ability, all of which can influence adult job attainment and performance and therefore socioeconomic status.

**Personality disorders.** Individuals with disruptive behavior disorders are at increased risk for cluster B personality disorders (i.e., antisocial, borderline, histrionic, or narcissistic personality disorder), and children with ADHD are at increased risk for antisocial personality disorder and borderline personality disorder in adulthood.

Dr. Newcorn described a longitudinal study in which the development of personality disorders in children with ADHD was tracked through adolescence and young adulthood. Increased rates of neuroticism and lower levels of conscientiousness and agreeableness were found in those with ADHD compared with matched controls. This was particularly the case among those whose ADHD was persistent, raising the question whether successful treatment of ADHD might decrease the risk of developing personality disorders.

**Conclusion**

Dr. Newcorn advised that clinicians assess patients with ADHD for comorbid disorders and assess patients with other psychiatric disorders for ADHD. Adults who have undiagnosed ADHD may visit a physician because of problems associated with a comorbid disorder, while children are more often brought in specifically for problems that relate to ADHD. He observed that it is important to identify comorbidity when it is present because comorbid disorders can affect the presentation and course of ADHD. In addition, comorbid disorders often require treatment independent of the treatment for ADHD. Distinguishing comorbidity from impairment secondary to ADHD can be difficult but is possible if clinicians understand the developmental course of the different conditions and take a detailed history.

Dr. Newcorn remarked that, because treatment of ADHD may have an impact on both the frequency and clinical manifestation of other disorders, the early identification and treatment of ADHD hopefully can alter the developmental course of both ADHD and these other disorders. While empirical data do not yet support this contention, prevention of comorbidity remains an appropriate goal of ADHD treatment as well as a potentially important direction for future research.

**Safety and Efficacy of Stimulant and Nonstimulant Treatments for ADHD and Comorbid Disorders**

Lenard A. Adler, M.D., first explained that 2 main classes of medication are used in the treatment of ADHD: stimulants and nonstimulants. Stimulants are either methylphenidate or amphetamine compounds; nonstimulant therapy is atomoxetine, a nor-epinephrine reuptake inhibitor. Two stimulants, mixed amphetamine salts extended-release (XR) and dexmethylphenidate XR, have U.S. Food and Drug Administration (FDA) approval for the treatment of ADHD in adults; the prodrug stimulant lisdexamfetamine has also received FDA approval. Atomoxetine is the only nonstimulant approved by the FDA for the treatment of adults with ADHD.

**Pharmacotherapy for ADHD Alone**

**Stimulants.** Studies of stimulants in adult ADHD have examined the efficacy of methylphenidate and amphetamine salts in immediate-release and extended-release formulations in adults with ADHD. The immediate-release forms have a duration of effect of 4 to 6 hours, whereas the extended-release forms have a duration of effect between 10 and 14 hours.

Dr. Adler cited a randomized study that examined immediate-release methylphenidate or placebo. Reductions in ADHD symptoms with the active drug started at week 1, were statistically significant (p < .001) versus placebo response at week 2, and continued through week 6. The response rate for methylphenidate was 76% versus 19% for placebo.

Immediate-release mixed amphetamine salts were also found to be effective in adults with ADHD. In a study that examined immediate-release mixed amphetamine salts versus placebo in a cohort of 27 adults with ADHD for 3 weeks, significant effects were found by week 2 and continued through week 3 (p < .001). The response rate for the active drug was 70% versus 7% for placebo.

Dr. Adler next presented data on sustained-release medications. Treatment with mixed amphetamine salts XR in 255 adults with ADHD was examined in a dose-ranging, multicenter, double-blind registration study. After 4 and 12 hours, mixed amphetamine salts XR showed a statistically significant reduction in scores on the CAARS Short Version Self-Report (p < .05). Over the 4-week course of treatment, statistically significant improvement versus placebo was found on the ADHD-Rating Scale (ADHD-RS) (≤ .001). However, a stepwise incremental improvement did not occur, and Dr. Adler noted that the package insert states that doses above 20 mg/day have not shown adequate evidence of providing additional benefit.

Another extended-release stimulant that has been studied in adults with ADHD is dexmethylphenidate. Spencer and colleagues examined several doses of dexmethylphenidate XR (20, 30, and 40 mg/day) versus placebo for 5 weeks and found a statistically significant mean change from baseline to endpoint on DSM-IV ADHD-RS total scores for all the doses studied (p = .006, p = .012, and p < .001, respectively).

**OROS methylphenidate** is an extended-release preparation of methylphenidate with an osmotic-release mechanism, which is thought to reduce the potential for abuse. The efficacy
of this stimulant in 72 adults with ADHD was compared with that of placebo in 77 adults. Over the 6 weeks of treatment with OROS methylphenidate, scores on the Adult ADHD Investigator Symptom Report Scale (AISRS) were significantly reduced, starting at week 3 (p = .04) and continuing to week 6 (p < .001).

Lisdexamfetamine, a therapeutically inactive prodrug that releases over 8 hours and has an absorption rate between immediate- and extended-release formulations of amphetamine products, was approved by the FDA in 2007 for use in children with ADHD. Two well-designed studies of lisdexamfetamine in children produced improvements in ADHD symptoms compared with placebo. In 2008, FDA approval was given for lisdexamfetamine use in adults with ADHD. Unpublished data for lisdexamfetamine use in adults with ADHD were presented at the 54th annual meeting of the American Academy of Child and Adolescent Psychiatry.

Dr. Adler stressed that any agent that has therapeutic effects can also have side effects. Common side effects of methylphenidate and amphetamine stimulants include dry mouth, insomnia, appetite suppression, headache, and a general sense of edginess. Patients with ADHD may have difficulty with sleep prior to beginning stimulant therapy, and sometimes stimulant therapy can exacerbate sleep difficulties. Occasionally, stimulant medications will uncover a motor or vocal tic. The FDA has placed warnings on all approved stimulant and nonstimulant ADHD medications regarding the need for careful monitoring in patients with preexisting cardiovascular conditions because all of these agents can cause modest changes in blood pressure and heart rate; however, some patients may have greater changes. Finally, these agents must also be monitored for abuse or misuse.

Nonstimulants. Next, Dr. Adler discussed a large registration study for atomoxetine involved 2 identical multisite, randomized, placebo-controlled trials with a total of 536 adults. The most frequently prescribed dose of atomoxetine was 90 mg/day. After 10 weeks of treatment, CAARS investigator-rated total scores showed significant effects of atomoxetine over placebo in both trials (p = .005 and p = .002).

Side effects that were observed more commonly with atomoxetine than with placebo included dry mouth, insomnia, nausea, decreased appetite, constipation, decreased libido, erectile difficulty, and dizziness. Modest increases in blood pressure and heart rate were also observed.

Nonpharmacologic Treatment for ADHD

Dr. Adler explained that nonpharmacologic treatments can be important in adults with ADHD. Safren and colleagues examined the use of cognitive-behavioral therapy (CBT) in adults with ADHD who were partially responsive to medication. Ongoing medication alone was compared with medication plus CBT. Patients who received CBT plus ongoing medication had less depression and anxiety and were more likely to be responders (56% versus 13% of the medication alone group, p < .02). For patients who have not completely responded to a pharmacologic intervention, CBT could be an effective augmentation strategy.

Pharmacotherapy for ADHD With a Comorbid Mental Health Disorder

Dr. Adler stated that in general, few data are available on the treatment of ADHD and comorbidities, and in some instances, the only data available are from studies in children and adolescents. When patients have ADHD and a comorbid disorder, clinicians have to decide which disorder to target first. The general rule is to treat the most impairing disorder first. For example, if a patient has ADHD and MDD with suicidal ideation, the clinician would treat the depression first because of its acuity; although ADHD can be impairing, it is a lifelong disorder and may present less of an acute concern than the depression.

Substance use disorders. The risk of exacerbating SUD in ADHD patients by treating them with stimulants was recently reviewed. Wilens stated that although childhood ADHD is a risk factor for adult SUD, stimulant treatment reduces the risk for cigarette smoking and SUD in adulthood. Wilens recommended that, when treating a patient with active SUD, the clinician allow for 1 week to 1 month of abstinence before assessing ADHD symptomatology. Dr. Adler stressed that stimulants carry warnings regarding abuse liability.

A naturalistic observation of treatment with bupropion sustained-release (SR) was conducted in 14 adolescents with ADHD who also had SUD and mood disorders. The researchers found improvement in major depression and reduction in drug use and ADHD symptomatology. An open-label investigation of 13 nondepressed adolescents with ADHD, conduct disorder, and SUDs found significant improvement in ADHD symptoms after 5 weeks of treatment with bupropion, up to a dose of 300 mg/day (mean Clinical Global Impressions Severity of Illness decline, p < .002).

A 3-month, double-blind, placebo-controlled study of atomoxetine in adults with ADHD and SUD showed significant effects from baseline (p < .001) of atomoxetine for ADHD. Patients with ADHD who had become abstinent from alcohol 4 to 30 days earlier were treated with atomoxetine or placebo for 12 weeks. Patients taking atomoxetine had significantly reduced ADHD symptoms as measured by the AISRS total score versus placebo (p = .007). Although the groups did not differ in time to relapse of heavy drinking, the patients taking atomoxetine had a 26% reduction in cumulative heavy drinking days.

Mood disorders. Treatment with a combination of fluoxetine and methylphenidate was found to be effective in an 8-week open study of 32 children and adolescents with ADHD and MDD
uptake inhibitor atomoxetine was re-

tantidepressant, the norepinephrine re-

prove the ADHD symptoms and the

disorders. The researchers noted that

lants was effective for these comorbid

with a variety of different psychostimu-

combination of fluoxetine or sertraline

with ADHD and MDD found that a

study 47 of 7 adolescents and 4 adults

alone (Table 4). Further, a naturalistic

adequate response to methylphenidate

or dysthymia who had not shown

adequate response to methylphenidate

alone (Table 4). Further, a naturalistic

study 47 of 7 adolescents and 4 adults

with ADHD and MDD found that a

combination of fluoxetine or sertraline

with a variety of different psychostimu-

lants was effective for these comorbid

disorders. The researchers noted that

the antidepressants did not seem to im-

prove the ADHD symptoms and the

stimulants did not seem to improve the
depressive symptoms. Although not an

antidepressant, the norepinephrine re-

uptake inhibitor atomoxetine was re-

cently found to improve ADHD but

not depression ratings compared with

placebo in 142 adolescents with ADHD

and major depression. 48

Few data are available for treating

ADHD and comorbid bipolar disorder in

adults. One study 49 of adolescents

and children found that after bipolar

symptoms were stabilized with dival-

proex, adjunctive mixed amphetamine

salts could be used to treat the comor-

bid ADHD symptoms.

Anxiety disorders. Dr. Adler re-

ported that data are lacking for the treat-

ment of adult ADHD with comorbidity

anxiety disorders. However, in patients

8 to 17 years of age who had ADHD

and anxiety disorders, a 12-week study 50

showed significant improvement in

both anxiety symptoms (p = .011) and

ADHD symptoms (p < .001) with atomoxetine versus placebo.

Sleep disorders. Dr. Adler stated that

the use of α2-agonists in children who

have both ADHD and sleep disorders

has been studied, 51 but few data exist

for adults. A chart review 52 (Figure 3)

of 14 patients aged 12 to 47 years with

ADHD and stimulant-associated

insomnia found significantly (p < .0001)

reduced insomnia in those treated with

adjunctive mirtazapine. A multicenter

trial of an extended release version of

the α2-agonist guanfacine (2–4 mg/day)

showed significant improvement in

ADHD symptoms versus placebo in

345 children and adolescents with

ADHD but without pre-existing sleep

disorders (2 mg, p = .0002; 3–4 mg, p = .0001). 53

Conclusion

Dr. Adler concluded that stimulant and

nonstimulant medications are ef-
fective for ADHD in adults and gener-

ally well tolerated, but patients should

be monitored for cardiovascular effects

and, with some stimulants, misuse or

abuse. Some data show efficacy for

CBT augmentation for patients with

ADHD who do not fully respond to

medication therapy. Other data show

efficacy of pharmacotherapy for comor-

bid psychiatric disorders in patients

with ADHD. In some instances, clinici-

ans may need to treat the comorbid

psychiatric condition before treating

ADHD.

Drug names: amphetamine/dextroamphetamine

(Adderall and others), atomoxetine (Strattera),
buproprion (Wellbutrin, Aplenzin, and others),
dexmethylphenidate (Focalin and others), divalproex
(Depakote), fluoxetine (Prozac and others),
guanfacine (Tenex and others), lisdexamfetamine
(Vyvanse), methylphenidate (Ritalin, Concerta, and
others), mirtazapine (Remeron and others), sertraline
(Zoloft and others).

Disclosure of off-label usage: The chair has
determined that, to the best of his knowledge,
amphetamine/dextroamphetamine, buproprion,
dexmethylphenidate, and methylphenidate are
not approved by the U.S. Food and Drug
Administration for the treatment of adult attention
deficit-hyperactivity disorder (ADHD); atomoxetine
is not approved for the treatment of childhood
anxiety disorders, major depression, and ADHD;
divalproex is not approved for the treatment of
ADHD and bipolar disorder; fluoxetine is not
approved for the treatment of ADHD and major
depression/dysthymia; mirtazapine is not approved
for the treatment of insomnia; sertraline is not
approved for the treatment of ADHD and major
depression; and guanfacine is not approved for the
treatment of childhood ADHD.

References


prevalence and correlates of adult ADHD in the

United States: results from the National Comor-

bidty Disorder Epidemiology Study Replication.

Am J Psychiatry 2006;163:716–723


national prevalence and correlates of adult

attention-deficit hyperactivity disorder. Br J

Psychiatry 2007;191:402–409

3. Barkley RA. Major life activity and health

outcomes associated with attention-deficit/

hyperactivity disorder. J Clin Psychiatry

2002;63(suppl 12):10–15


reports of diagnosed ADHD: a controlled study of 1001 adults in the community.
16. Ken L, Craven D. Do we have a relationship between attention deficit hyperactivity disorder and bipolar disorder? J Affect Disord 2003;73:211–221
17. Faraone SV, Biederman J. Do attention deficit hyperactivity disorder and major depression share familial risk factors? J Nerv Ment Dis 1997;185:533–541