

# Current Strategies in the Diagnosis and Treatment of Childhood Attention-Deficit/Hyperactivity Disorder

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Symptoms of childhood attention-deficit/hyperactivity disorder affect cognitive, academic, behavioral, emotional, social, and developmental functioning. Attention-deficit/hyperactivity disorder is the most commonly diagnosed neurodevelopmental disorder in children and adolescents. An estimated 2 to 16 percent of school-aged children have been diagnosed with the disorder. The prevalence of attention-deficit/hyperactivity disorder in the primary care setting is similar to that in the general community, depending on the diagnostic criteria and population studied. The causality of attention-deficit/hyperactivity disorder is relatively unknown. Most recent studies focus on the role of dopamine; norepinephrine; and, most recently, serotonin neurotransmitters. The disorder is classified into three general subtypes: predominantly hyperactive-impulsive, predominantly inattentive, and combined. Screening tools and rating scales have been devised to assist with the diagnosis. Appropriate treatment can dramatically improve the function and quality of life of the patient and family. Pharmacologic treatment includes stimulants, such as methylphenidate and mixed amphetamine salts, or nonstimulants, such as atomoxetine. Behavioral approaches, particularly those that reward desirable behavior, are also effective. A combination of pharmacologic and behavioral therapies is recommended. (*Am Fam Physician*. 2009;79(8):657-665. Copyright © 2009 American Academy of Family Physicians.)



ILLUSTRATION BY MARK E. SCHULER

► See related editorial on page 640.

► Patient information: A handout on ADHD in children, written by the authors of this article, is available at <http://www.aafp.org/afp/20090415/657-s1.html>

**A**ttention-deficit/hyperactivity disorder (ADHD) is a chronic, neurobiologic, behavioral disorder that affects 2 to 16 percent<sup>1</sup> of school-aged children, depending on the diagnostic criteria and population studied (e.g., primary care versus referral).<sup>2</sup> The symptoms of ADHD affect cognitive, academic, behavioral, emotional, social, and developmental functioning.

## Etiology

Although there are many theories, no single etiology for ADHD has been substantiated. A number of risk factors that affect a child's brain development and behavior may lead to ADHD symptoms. These risk factors include genetic factors, behavioral disorders, medical conditions that affect brain development,

and various environmental influences on the developing brain (e.g., toxins such as lead and alcohol; nutritional deficiencies).<sup>3</sup>

The neurotransmitters dopamine and norepinephrine have been implicated in the pathophysiology of ADHD. Dopamine influences behaviors, such as risk taking and impulsivity, whereas norepinephrine modulates attention, arousal, and mood. Although dopamine and norepinephrine are likely involved in the pathophysiology of ADHD, further study is needed.<sup>4</sup> Current research suggests that rather than acting specifically on dopamine, stimulants create a calming effect by increasing serotonin levels. The new generation of compounds that interact more specifically with the serotonin system may prove to be safer and more effective for ADHD treatment. Likewise, children who

**SORT: KEY RECOMMENDATIONS FOR PRACTICE**

| Clinical recommendation   | Evidence rating | References                               |
|---|-----------------|--|
| A proper diagnosis of ADHD requires obtaining information from teachers, family members, and non-family members who are familiar with the child's behavior. | C               | 7, 8, 12, 20, 21, 32                     |
| Pharmacotherapy with stimulant medication is the first-line treatment for most patients with ADHD.  | A               | 8, 10, 12-14, 20, 21, 31, 32, 35, 36, 39 |
| On average, carefully monitored pharmacotherapy is more effective for ADHD than intensive behavioral treatment alone.                                       | B               | 44                                       |
| Support groups for parents who have children with ADHD help parents connect with others who have children with similar problems.                            | B               | 3, 12                                    |

ADHD = attention-deficit/hyperactivity disorder.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

**Table 1. Combined AAP and AACAP Recommendations for the Evaluation of Children with Suspected ADHD**

**Recommendation 1:** The primary care physician should initiate an evaluation for ADHD in a child six to 12 years of age who presents with inattention, hyperactivity, impulsivity, academic underachievement, or behavioral problems. The initial evaluation should include the following: (1) standard history and physical examination, with the AACAP recommending assessment of the child's developmental history, hearing and vision, any learning difficulties or psychiatric illness, and family history of ADHD; (2) neurologic examination; (3) family assessment, with the AACAP recommending review of family stressors and family coping style; and (4) school assessment (see recommendation 4).

**Recommendation 2:** The diagnosis of ADHD requires that a child meet DSM-IV diagnostic criteria for the disorder (Table 2).

**Recommendation 3:** The assessment of ADHD requires evidence obtained directly from parents or caregivers regarding the core symptoms of ADHD in various settings, age at onset of symptoms, duration of symptoms, and degree of functional impairment.

**Recommendation 4:** The assessment of ADHD requires evidence obtained directly from the classroom teacher (or other school-based professional) regarding the core symptoms of ADHD, duration of symptoms, degree of functional impairment, and coexisting conditions. A physician should review any reports from a school-based multidisciplinary evaluation, including assessments from the child's teacher or other school-based professional.

**Recommendation 5:** The evaluation of a child with ADHD should include an assessment for coexisting conditions (e.g., learning and language disabilities, oppositional defiant disorder, conduct disorder, anxiety and depression).

**Recommendation 6:** Diagnostic testing (e.g., measurement of lead and thyroid hormone levels; neuroimaging; electroencephalography) is not routinely recommended.

NOTE: Use of ADHD-specific assessment scales (Table 6) is a clinical option when evaluating a child for ADHD, but is not recommended in the diagnosis of the disorder.

AACAP = American Academy of Child and Adolescent Psychiatry; AAP = American Academy of Pediatrics; ADHD = attention-deficit/hyperactivity disorder; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th ed.

Information from references 7 and 8.

have been diagnosed with ADHD and who have undergone functional brain imaging in the basal ganglia and anterior frontal lobe may have reduced global and local activation in these areas.<sup>5</sup> Although ADHD was thought to predominantly affect boys, more recent studies have shown no association between a child's sex and the disorder. There is also no correlation between a child's sex and cognitive, psychosocial, school, or family functioning.<sup>6</sup>

## Diagnosis

### CLINICAL PRESENTATION

Typically, a child with ADHD initially presents to a primary care physician at the request of parents or teachers who are unable to manage the child's behavior. To make an accurate diagnosis, it is imperative to elicit information about the child's ongoing aberrant behavior not only from family members, but also from non-family members who are familiar with the child.<sup>1</sup> Table 1 presents recommendations for the evaluation of children with suspected ADHD from the American Academy of Pediatrics (AAP) and the American Academy of Child and Adolescent Psychiatry (AACAP).<sup>7,8</sup> Behaviors, such as inattentiveness, hyperactivity, and impulsivity, are specifically included in the AAP and AACAP recommendations and in the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) criteria for ADHD (Table 2).<sup>9</sup> To be diagnosed with ADHD based on the DSM-IV criteria, a child must display at least six of the nine symptoms of either inattention or hyperactivity-impulsivity. The symptoms must be evident in discrete

**Table 2. DSM-IV Criteria for the Diagnosis of ADHD**

A. Either 1 or 2:

1. Six (or more) of the following symptoms of **inattention** have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental level:

*Inattention*

- Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities
- Often has difficulty sustaining attention in tasks or play activities
- Often does not seem to listen when spoken to directly
- Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)
- Often has difficulties organizing tasks and activities
- Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework)
- Often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, tools)
- Is often easily distracted by extraneous stimuli
- Is often forgetful in daily activities

2. Six (or more) of the following symptoms of **hyperactivity-impulsivity** have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental level:

*Hyperactivity*

- Often fidgets with hands or feet, or squirms in seat
- Often leaves seat in classroom or in other situations in which remaining seated is expected
- Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)
- Often has difficulty playing or engaging in leisure activities quietly
- Is often "on the go" or acts as if "driven by a motor"
- Often talks excessively

*Impulsivity*

- Often blurts out answers before questions have been completed
- Often has difficulty awaiting turn
- Often interrupts or intrudes on others (e.g., butts into conversations or games)

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before seven years of age

C. Some impairment from the symptoms is present in two or more settings (e.g., at school or work and at home)

D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning

E. The symptoms do not occur exclusively during the course of a pervasive developmental disorder, schizophrenia, or other psychiatric disorder and are not better accounted for by another mental disorder (e.g., mood disorder, anxiety disorder, dissociative disorder, a personality disorder)

ADHD = attention-deficit/hyperactivity disorder; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th ed.

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settings, persist for more than six months, and begin before seven years of age.<sup>9</sup>

The DSM-IV criteria divides the disorder into three general subtypes: predominantly hyperactive-impulsive, predominantly inattentive, and combined. A child with the predominantly hyperactive-impulsive type is excessively fidgety and restless, seems to always be "on the go," and has difficulty waiting and remaining seated. The child may act immaturely, may not set physical boundaries, and may exhibit destructive behaviors.<sup>3</sup> The combination of impulsivity and hyperactivity seems particularly common in younger children.<sup>10</sup> The predominantly inattentive type has several characteristics, including easy distractibility, forgetfulness, daydreaming, disorganization, poor concentration, losing or misplacing things, and difficulty completing tasks (e.g., classroom assignments, homework). A child with the combined type typically exhibits many of the behaviors of the other two subtypes.<sup>11</sup>

By adolescence, the hyperactivity associated with ADHD wanes and the consequences of childhood ADHD become evident, including the development of coexisting problems. Problems related to ADHD that may manifest during adolescence include antisocial behavior, cognitive fatigue, difficulties at school or work, ineffective self-monitoring, legal trouble, low self-esteem, impulsivity, risk taking, and substance abuse.<sup>12,13</sup>

## Evaluation

Because there are no definitive laboratory tests for ADHD, it is considered a clinical diagnosis. Diagnostic tests (e.g., lead levels, thyroid hormone levels, neuroimaging, electroencephalography) are not needed to establish the diagnosis of ADHD, but they may be warranted based on specific history and physical examination findings.<sup>14</sup> The symptoms of ADHD overlap with those of learning disabilities and mental health conditions, and coexisting conditions are common in persons with ADHD (*Table 3*).<sup>13,15-19</sup> *Table 4* includes questions that may help detect coexisting conditions.<sup>20</sup> Children with ADHD should also be examined for other medical, psychiatric, and environmental

conditions.<sup>7,13</sup> *Table 5* presents the differential diagnosis of ADHD.<sup>20</sup>

The assessment of children with suspected ADHD requires information obtained directly from parents

or caregivers about the core symptoms in various settings, age at onset of symptoms, duration of symptoms, and degree of functional impairment.<sup>21</sup> The following questions, devised by the AAP, may be used as an initial

**Table 3. Prevalence of Coexisting Conditions in Persons with ADHD**

| Coexisting condition          | Persons with ADHD who have the coexisting condition (%) |
|-------------------------------|---|
| Anxiety                       | 25  |
| Conduct disorder              | 10 to 20  |
| Developmental disorder        | 10 to 90  |
| Mood disorder                 | 15 to 75  |
| Oppositional defiant disorder | 35 to 65  |
| Substance abuse               | 20 to 40  |
| Tic                           | 50  |

ADHD = attention-deficit/hyperactivity disorder.

Adapted with permission from *New developments in the treatment of attention-deficit/hyperactivity disorder in primary care*. Prim Care Companion J Clin Psychiatry. 2006;8(4):227, with additional information from references 15 through 19.

**Table 4. Screening Questions to Detect Coexisting Conditions in Children with ADHD**

**Conduct disorder**

Is the child violent or cruel toward people or animals?  
Has the child deliberately destroyed others' property?  
Does the child steal?  
Has the child been involved in delinquent behavior?

**Depression**

Does the child worry or cry excessively?  
Does the child have recurrent thoughts of death or suicide?

**Oppositional defiant disorder**

Does the child argue with adults and actively defy rules?  
Does the child often lose his or her temper?

**Possible sexual abuse**

Does the child exhibit inappropriate sexual behavior?

**Tourette syndrome**

Does the child show repetitive vocal or motor tics?

NOTE: Positive responses should prompt more formal assessment for the disorders.

ADHD = attention-deficit/hyperactivity disorder.

Adapted with permission from Smuck WD, Hedayat M. Evaluation and treatment of ADHD. Am Fam Physician. 2001;64(5):823.

**Table 5. Differential Diagnosis of ADHD**

**General medical conditions (biomedical)**

Adverse effects from medication use (e.g., bronchodilators, corticosteroids, isoniazid, antipsychotics, antihistamines, decongestants, beta agonists, anticonvulsants)

Allergic rhinitis

Asthma

Hypothyroidism

Infection or trauma

Lead toxicity

Malnutrition

Sensory impairment (vision, hearing)

Sequelae of the central nervous system

**Neurologic conditions (emotional or psychiatric)**

Brain injury

Developmental delays

Learning disability

Mental retardation (e.g., fetal alcohol syndrome, fragile X syndrome, phenylketonuria)

Seizure disorder

Sleep disorders, such as obstructive sleep apnea

Speech or language problems (e.g., expressive/receptive and phonologic disorders, dysfluency, apraxia)

**Psychiatric conditions**

Anxiety

Conduct disorder

Depression

Obsessive-compulsive disorder

Oppositional defiant disorder

Posttraumatic stress disorder

Substance abuse

**Environmental conditions (family psychosocial problems)**

Child neglect, physical or sexual abuse

Dysfunctional parenting (e.g., inappropriate, inconsistent, punitive)

History of bullying, victim of bullying

Improper learning environment (e.g., unsafe, disruptive)

Parental psychopathology or substance abuse

Social skills deficits

Sociocultural factors

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Adapted with permission from Smuck WD, Hedayat M. Evaluation and treatment of ADHD. Am Fam Physician. 2001;64(5):823.

**Table 6. Ratings Scales Used in the Evaluation of Childhood ADHD**

| Rating scale  | Behaviors/conditions assessed   |
|---|---|
| <b>Broadband assessments</b>  |   |
| Behavior Assessment System for Children <sup>22</sup>                     | Hyperactivity; aggression; conduct problems; anxiety; depression; somatization; atypicality; withdrawal; attention problems; learning problems; lack of adaptability; lack of social, leadership, or study skills   |
| Child Behavior Checklist/Teacher Report Form <sup>23,24</sup>             | Somatic complaints; social, thought, and attention problems; anxiety; depression; aggressive or delinquent behavior; withdrawal   |
| Conners Rating Scales (long form) <sup>25</sup>                           | Oppositional behavior; cognitive problems; hyperactivity; anxiousness/shyness; perfectionism; social problems; psychosomatic illnesses; restlessness/impulsiveness; emotional lability; DSM-IV symptoms scale, inattentive symptoms, and hyperactive-impulsive symptoms |
| <b>Narrowband assessments</b>   |   |
| ADHD Rating Scale <sup>26</sup>   | DSM-IV symptoms of ADHD   |
| Behavior Assessment System for Children—Monitor for ADHD <sup>22,27</sup> | Problems with attention, adapting, and internalizing; hyperactivity   |
| Childhood Attention Problems Scale <sup>28</sup>                          | Attention problems, impulsivity, hyperactivity  |
| Comprehensive Teacher's Rating Scale <sup>29</sup>                        | Attention problems, hyperactivity, lack of social skills, oppositional behavior   |
| Conners Rating Scales (short form) <sup>25</sup>                          | Oppositional behavior, cognitive problems, hyperactivity, ADHD Index  |
| Disruptive Behavior Rating Scale <sup>30</sup>                            | DSM-IV symptoms of ADHD, compulsive disorder  |
| Vanderbilt Assessment Scales <sup>30</sup>                                | DSM-IV symptoms of ADHD; comorbid conditions, such as oppositional defiant disorder, conduct disorder, anxiety, depression  |
| <b>Assessment of medication adverse effects</b>                           |   |
| Side Effects Rating Scale <sup>30</sup>                                   | Sleeping problems, appetite problems, staring or daydreaming, withdrawal, anxiety, irritability, somatic complaints, emotional lability, dizziness, tics  |

NOTE: *These scales may be used in the evaluation of ADHD, but are not recommended in the diagnosis of the condition.*

ADHD = attention-deficit/hyperactivity disorder; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th ed.

Information from references 22 through 30.

screening test: How is your child doing in school? Are there any problems with learning that you or the teachers have noticed? Is your child happy in school? Are you concerned with any behavioral problems in school, at home, or when your child is playing with friends? Is your child having problems completing classwork or homework?<sup>7</sup>

Table 6 lists assessment scales for ADHD.<sup>22-30</sup> Screening tests that draw on information reported by the parents may be more suitable for primary care physicians than those requiring direct observation or elicitation of developmental skills.

### Treatment

Pharmacologic and behavioral approaches are effective in the treatment of ADHD, particularly when combined. A tool kit has been developed by the AAP and the National Initiative for Children's Healthcare Quality to help physicians improve the management of ADHD. The free tool kit is available at <http://www.nichq.org/adhd.html>. AAP guidelines suggest follow-up visits for children with ADHD to review goals, medications, behavioral changes, and the child's development.<sup>7</sup>

### PHARMACOLOGIC THERAPY

Primary care physicians should be familiar with the multiple medications available to treat ADHD (Table 7).<sup>31,32</sup> Stimulant medications are first-line agents.<sup>32</sup> Atomoxetine (Strattera) is a second-line agent and has been shown to be effective in placebo-controlled trials.<sup>33,34</sup> Other medications with less extensive evidence to support their use include bupropion (Wellbutrin), alpha<sub>2</sub>-agonists, and tricyclic antidepressants.<sup>35</sup>

For the past 40 years, stimulants (methylphenidate [Ritalin] and mixed amphetamine salts) have been the mainstay of ADHD therapy, although there is no evidence supporting the use of one stimulant over another.<sup>36,37</sup> Short-, intermediate-, and long-acting preparations have similar effectiveness. Administration of short-acting preparations can be timed to correspond with certain activities. Long-acting formulations eliminate the burden of medication administration during the school day, improve compliance, and decrease opportunity for abuse.

Treatment should be initiated at low dosages and then titrated over two to four weeks until an adequate response is achieved or unacceptable adverse effects occur. If one

**Table 7. Pharmacologic Treatment of Attention-Deficit/Hyperactivity Disorder**

| Drug                                       | Brand names   | Initial dosage  | Usual dosage  | Maximal dosage (per day) |
|--|---|---|---|--------------------------|
| <b>First-line agents (stimulants)</b>      |   |   |   |                          |
| Methylphenidate                            |   |   |   |                          |
| Immediate release                          | Ritalin, Methylin   | 5 mg twice per day  | 10 to 20 mg two to three times per day  | 60 mg                    |
| Extended release                           | Ritalin SR, Metadate ER, Methylin ER  | 10 mg twice per day, or 20 mg once per day  | 20 to 40 mg once per day, or 40 mg in the morning and 20 mg in the early afternoon      | 60 mg                    |
| Long acting                                | Ritalin LA, Metadate CD<br>Concerta<br>Daytrana (patch worn nine hours per day) | 20 mg once per day<br>18 mg every morning<br>10 mg                                      | 20 to 40 mg once per day<br>18 to 54 mg every morning<br>10 to 30 mg                    | 60 mg<br>72 mg<br>30 mg  |
| Dexmethylphenidate                         | Focalin   | 2.5 mg twice per day  | 5 to 10 mg twice per day  | 20 mg                    |
| Dextroamphetamine                          |   |   |   |                          |
| Short acting                               | (formerly Dextrostat)   | 2.5 mg twice per day  | 5 to 15 mg twice per day, or 5 to 10 mg three times per day                             | 40 mg                    |
| Intermediate acting                        | Dexedrine Spansule, Adderall*   | 5 mg once or twice per day  | 5 to 30 mg once per day, or 5 to 15 mg twice per day                                    | 40 mg                    |
| Long acting                                | Adderall XR*  | 10 mg once per day  | 10 to 30 mg once per day  | 30 mg                    |
| <b>Second-line agents</b>                  |   |   |   |                          |
| Atomoxetine                                | Strattera   | 10 to 18 mg once per day  | 18 to 60 mg once per day  | 100 mg                   |
| <b>Third-line agents</b>                   |   |   |   |                          |
| Bupropion (sustained and extended release) | Wellbutrin  | 100 to 150 mg twice per day (sustained release); 150 mg once per day (extended release) | 150 mg twice per day (sustained release); 150 to 300 mg once per day (extended release) | 300 mg                   |
| Imipramine                                 | Tofranil  | 30 to 40 mg once per day  | 37.5 to 75 mg twice per day   | 150 mg                   |
| Desipramine                                | Norpramin   | 25 mg once or twice per day   | 50 mg twice per day, or 100 mg once per day   | 150 mg                   |
| Clonidine                                  | Catapres  | 0.025 to 0.05 mg per day  | 0.1 to 0.3 mg per day, divided into three or four doses                                 | 0.4 mg                   |
| Guanfacine                                 | Tenex   | 0.5 mg per day  | 0.5 to 4 mg per day, divided into two to four doses                                     | 4 mg                     |

\*—Dextroamphetamine combined with amphetamine salts.

Adapted with permission from Dopheide JA. ASHP therapeutic position statement on the appropriate use of medications in the treatment of attention-deficit/hyperactivity disorder in pediatric patients. *Am J Health Syst Pharm*. 2005;62(14):1504, 1506, with additional information from reference 32.

stimulant is not effective, another should be attempted before second-line medications are considered. Although some children benefit from daily psychostimulant therapy, weekend and summer “drug holidays” are suggested for children whose ADHD symptoms predominantly affect schoolwork or to limit adverse effects (e.g., appetite suppression, abdominal pain, headache, insomnia,

irritability, tics). Adverse effects also may be minimized by taking the medication with food or by adjusting the dosage. The U.S. Food and Drug Administration (FDA) has added warnings to psychostimulant labels linking the medications with increased risk of sudden death and cardiovascular problems, including heart attacks. Delays in growth are also possible with chronic stimulant ther-

## Adverse effects

Appetite suppression and weight loss, abdominal pain, headache, irritability, growth effects, tics, cardiovascular effects, insomnia

Same as other methylphenidate brands; skin irritation and rash

Same as methylphenidate; causes fewer headaches, but more stomach pain than methylphenidate

Same as methylphenidate

Similar to methylphenidate; nausea, vomiting, fatigue, mild increase in blood pressure and pulse

Weight loss, insomnia, agitation, anxiety, dry mouth, seizures

Anticholinergic effects, dry mouth, constipation, tachycardia, changes on electrocardiography, sudden death, arrhythmias

Same as imipramine

Drowsiness, dizziness, dry mouth, orthostatic hypotension

Same as clonidine, but lower incidence and severity

apy, although some studies indicate that long-term effects are minimal.<sup>36,38</sup>

Atomoxetine, a selective norepinephrine-reuptake inhibitor, is the first nonstimulant medication approved by the FDA for the treatment of ADHD. Atomoxetine should be considered if the child is unresponsive to stimulants, the parents prefer a nonstimulant medication,

or there is concern about the patient or family members abusing stimulants. Although there are no studies that directly compare atomoxetine with stimulant medications, clinical trials comparing atomoxetine with placebo showed that the drug has comparable effectiveness to stimulant medications.<sup>33,34</sup> Atomoxetine can be administered once or twice daily but, unlike stimulants, must be given every day without drug holidays. Symptoms may decrease within one week of initiation of atomoxetine, although core ADHD symptoms are usually not affected for four to six weeks.

The FDA has added a warning to atomoxetine labels indicating that the medication should be discontinued in patients with jaundice or laboratory evidence of liver injury. This label change was based on two reported cases, both of which resolved after discontinuation of therapy.<sup>39</sup> A black box warning about the rare association between atomoxetine and suicidal ideation in children also has been added to the atomoxetine label. Patients taking atomoxetine should be monitored closely, especially in the first four weeks of therapy. The adverse effects are similar to those of stimulants and also include mild increases in pulse or blood pressure. Fatigue and nausea occur more often with atomoxetine than with stimulants, although these symptoms may not be as bothersome with bedtime administration.

Bupropion, a dopaminergic antidepressant, is an alternative treatment for ADHD. It may be a reasonable option in patients with coexisting mood disorders and in those who are unresponsive to stimulants. Although placebo-controlled trials have shown that bupropion is effective in adolescents with ADHD and coexisting depression, two small randomized trials comparing bupropion with methylphenidate reported a smaller therapeutic effect on core ADHD behavior and more adverse effects with bupropion.<sup>40,41</sup> Patients with a history of seizure disorders should not receive bupropion. Rare adverse effects include weight loss, insomnia, agitation, anxiety, and dry mouth.

The tricyclic antidepressants imipramine (Tofranil) and desipramine (Norpramin) have been shown to effectively control ADHD-related behavioral problems. Controlled trials have generally shown that tricyclic antidepressants have effects on core ADHD symptoms equal to those of stimulants.<sup>42</sup> Because of their potentially serious adverse effects, tricyclic antidepressants should be considered only when adequate trials of stimulant medications, atomoxetine, and behavioral interventions have failed.<sup>14,31</sup> Tricyclic antidepressants should be initiated at low doses and adjusted as necessary. Adverse effects include dry mouth; constipation; tachycardia; changes on electrocardiography; and, rarely, sudden death. Tricyclic anti-

depressant labels include a black box warning about the risk of suicidal ideation and behavior in children and adolescents.

The alpha<sub>2</sub>-agonists clonidine (Catapres) and guanfacine (Tenex) are occasionally used to treat ADHD, especially if the patient has conduct issues. The medications may also be used as adjuncts to stimulant medications because they counteract the insomnia and appetite suppression that often occur with stimulant use.<sup>43</sup> Clonidine should be initiated as a single, low dose at bedtime and slowly titrated over two to four weeks to minimize adverse effects. Clonidine should never be discontinued abruptly, but the dosage slowly tapered. Common adverse effects of clonidine and guanfacine include drowsiness, dizziness, dry mouth, and orthostatic hypotension.

### BEHAVIORAL INTERVENTIONS

There are a number of well-supported behavioral interventions for ADHD. Most behavioral approaches focus on rewarding desired behavior and applying consequences for unwanted behavior to gradually reshape the child's thinking and behavior.<sup>3</sup> For example, tokens or points may be given to the child to immediately reward good behavior or work. Interventions that help reinforce parental involvement include support groups, which connect parents who have children with similar problems, and parenting skills training, which gives parents techniques and tools for managing their child's behavior. Psychotherapy and cognitive behavior therapy have little or no documented effectiveness for the treatment of ADHD, mostly because of a lack of high-quality studies.<sup>14</sup>

### COMBINED THERAPY

A 14-month, multicenter, randomized study compared the effectiveness of multimodal treatment (combined behavioral interventions and pharmacotherapy) with either treatment alone.<sup>44</sup> A total of 579 children with ADHD were randomized to one of four treatment groups: pharmacotherapy, intensive behavioral treatment, combination of pharmacotherapy and intensive behavioral treatment, and standard care by community caregivers. The study showed that combination treatment and pharmacotherapy alone yielded similar results and were more effective than behavioral treatment alone or standard care in reducing core ADHD symptoms. The study also found that combining behavioral modifications and pharmacotherapy may reduce the need for higher medication dosages and may provide modest advantages for non-ADHD symptoms and positive functioning outcomes.

**EDITOR'S NOTE:** As this article was going to press, a study by Molina and colleagues was released questioning the long-term effectiveness of ADHD drug therapy. The study showed that there were no significant differences among pharmacologic, behavioral, and combined therapy groups after six to eight years, and that all children in the study had significant impairment compared with unaffected peers.—CAROLINE WELLBERY, MD

Molina BS, Hinshaw SP, Swanson JM, et al., for the MTA Cooperative Group. MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry*. 2009 [Epub ahead of print].

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