Attention-Deficit/Hyperactivity Disorder in Children

Editor:
Jerald Kay, MD
Professor and Chair, Department of Psychiatry
Wright State University School of Medicine
Dayton, OH

Contributors:
Christina G. Weston, MD
Assistant Professor, Department of Psychiatry
Associate Director, Division of Child and Adolescent Psychiatry
Wright State University School of Medicine
Dayton, OH

Suzie C. Nelson, MD
Junior Resident Instructor, Department of Psychiatry
Wright State University School of Medicine
Dayton, OH

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Cover Illustration by Kathryn K. Johnson
Attention-deficit/hyperactivity disorder (ADHD) is a common chronic disorder that occurs in up to 10% of boys and 5% of girls of elementary school age, although prevalence estimates vary. ADHD is characterized by pronounced difficulty in maintaining focused attention on tasks, hyperactivity, and impulsivity. Parents often focus on the difficulty children with ADHD have in acquiring academic skills; however, these children also have significant difficulties in social and family interactions. Success in school and with relationships is further compromised because children with ADHD are more likely to abuse substances and engage in delinquent behaviors. While once believed to be a childhood disorder that would likely resolve during puberty, it is estimated that 60% of patients with childhood ADHD continue to have significant symptoms into adulthood, resulting in further social and occupational difficulty. Adult outcomes of ADHD include lower educational and career attainment.

ADHD is thought to be caused by a combination of environmental, genetic, and biologic factors, though the exact etiology of this disorder is unknown. Higher rates of ADHD have been found in children with exposure to cigarettes and alcohol in utero, low birth weight, exposure to lead, and brain injuries occurring in utero. One study found that low parental education level was also a risk factor for ADHD, with this effect seen more often in boys. ADHD is known to run in families; between 10% and 35% of children with ADHD have a first-degree relative with past or present ADHD. A recent multicenter study demonstrated aggregation of symptoms in families of children diagnosed with ADHD; parents of children with ADHD had higher reports of inattention, hyperactivity, and impulsivity than parents of controls. Defects in several genes regulating dopamine, norepinephrine, and epinephrine have been associated with ADHD. The most widely confirmed gene association has been found to be the DRD4 gene defect, found in 30% of the general population and 50% to 60% of the population with ADHD. This defect creates a delay in translating dopamine signals. Both epinephrine and norepinephrine are agonists at DRD4, which explains how medications that affect either of these catecholamines can affect the dopamine system and improve ADHD symptoms. The “dopamine hypothesis” proposes that inadequate availability of dopamine in the central nervous system contributes to ADHD. The neurotransmitter dopamine is important in initiating purposeful movement, increasing motivation and alertness, reducing appetite, and inducing insomnia. Stimulants increase the availability of the neurotransmitter dopamine, and their success in treating ADHD helps to confirm the dopamine hypothesis.

ADHD is one of the most common psychiatric disorders of childhood and adolescence. Given its high prevalence in school-age children, it is likely that pediatricians and child and adolescent psychiatrists will see these children often. Given the chronic nature of the illness and estimates of frequent persistence of its sequelae into adulthood, clinicians will need to manage the treatment of these patients for many years beyond childhood. Therefore, it is important for all psychiatrists to be able to identify patients with ADHD and to be comfortable with diagnosing and managing the disorder.

CASE STUDY

INITIAL PRESENTATION

A 7-year-old first-grade boy is brought to the physician’s office by his mother. She reports that she is worried about her son’s behavior and that he doesn’t listen to her.

HISTORY

The patient’s mother had an uncomplicated pregnancy, and the patient was born full term without any birth complications. His mother did not drink alcohol or use illicit drugs while pregnant but did smoke cigarettes. The patient achieved developmental milestones at appropriate times. He has been treated only for infections and for occasional accidents. He required stitches
on one occasion after jumping off furniture and cutting his chin on a coffee table. During prior visits with the physician, the patient was noted to be very active, often attempting to dismantle the wall-mounted otoscope. The mother reports that her only child has always been “a handful.” He was expelled from his first preschool at age 3 years because he was disruptive, wouldn’t sit still for circle time, and would on occasion hit teachers or students when he didn’t get his way. His mother delayed his starting kindergarten until he was 6 years to give him time to mature. His kindergarten teacher noted last year that he couldn’t follow directions well, had a short attention span, and was very active. His current first-grade teacher reports difficulties in getting him to sit down to read. His mother states that he will not stay focused on any activity except his Game Boy for more than 15 minutes. He is frequently loud and destructive when he plays.

There is a family history of depression in the maternal grandmother, and the patient’s father is reported to have had been a “wild boy” when he was younger but was never treated for any mental health problems. The patient is on no prescription medications.

**Physical Examination**

On physical examination, the patient appears to be a well-developed child. Multiple small bruises on his shins are noted. He is in the 55th percentile for both height and weight. He would not cooperate with otoscopic examination. The remainder of the physical examination including neurologic examination is unremarkable, and vital signs are within normal limits.

On mental status examination, the patient is a cheerful young boy. He spends most of the time climbing on and off the exam table and exploring items throughout the room briefly. Attempts by his mother to get him to read a book or sit in her lap are unsuccessful. His speech is somewhat loud and fast. Mood is described as “good.” Affect appears happy, although he is somewhat labile when his mother scolds him for playing with the sink.

- **What is the differential diagnosis of behavior and attention problems in a young child?**

Several mental disorders are associated with behavioral problems in young children, with ADHD being the most common. Although children with other psychiatric disorders may present with symptoms that appear similar to ADHD, these patients will have other symptoms unique to the particular disorder. The defiance and refusal to follow adult requests seen in oppositional defiant disorder (ODD) can be similar to the not listening and impulsivity seen in ADHD. Conduct disorder, which is in the differential for ADHD, often presents with symptoms not seen in ADHD, such as severe aggression and inability to follow societal rules. Children who are depressed and/or anxious often are unable to pay close attention, and these disorders can be confused with inattentive ADHD. Childhood bipolar disorder often presents with hyperactivity-impulsivity and inattention in addition to other symptoms not seen in ADHD.

General medical causes need to be considered because poor attention and behavior also may be caused by impaired vision or hearing, seizures, sequelae of head trauma, acute or chronic medical illness, poor nutrition, or insufficient sleep. The spectrum of learning disorders, mental retardation, and borderline intellectual functioning often can present with ADHD symptoms. These problems can be difficult to identify in children in the early school years. It is important to remember that some children with attention/behavioral problems may simply have a difficult temperament or an activity level that is at the high end of normal. Children with difficult temperament may have more challenges when in a poor school setting or have parents unable to effectively manage their behaviors; when these improve, their problems improve. However, a child with ADHD will still have difficulty with effective schools and parenting.

- **How can the diagnosis be confirmed?**

The diagnosis of ADHD is a clinical one, made on the basis of a comprehensive history of symptoms causing impairment in several settings. The DSM-IV-TR criteria for ADHD are 6 or more symptoms of inattention and/or 6 or more symptoms of hyperactivity-impulsivity (Table 1). The symptoms must have been present before age 7 years and also occur in 2 or more settings. Symptoms must also have persisted for at least 6 months and be maladaptive and inconsistent with a child’s developmental level. A first-grader who is unable to sit and listen to a teacher’s lecture for 30 minutes would not be considered abnormal, whereas a high school student’s inability to listen to a lecture for 30 minutes would be considered developmentally inappropriate. There are 3 subtypes of ADHD, determined by the symptom pattern over the previous 6 months: predominantly inattentive type, predominantly hyperactive-impulsive type, and combined type.

The assessment of ADHD in a school-aged child requires a careful interview with the family to document the presence of multiple symptoms of inattention and hyperactivity-impulsivity. Information gathering can be done by direct interview of the parent and/or having him/her complete an ADHD-specific rating scale. Collateral history from the school also is required to
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Table 1. DSM-IV-TR Diagnostic Criteria for Attention-Deficit/Hyperactivity Disorder

A. Either (1) or (2):
   (1) 6 (or more) of the following symptoms of inattention have persisted for at least 6 months to a degree that it is maladaptive and inconsistent with developmental level:
   (a) often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities
   (b) often has difficulty sustaining attention in tasks or play activities
   (c) often does not seem to listen when spoken to directly
   (d) often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace
   (e) often has difficulty organizing tasks and activities
   (f) often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (eg, schoolwork or homework)
   (g) often loses things necessary for tasks or activities
   (h) is often easily distracted by extraneous stimuli
   (i) is often forgetful in daily activities
(2) 6 (or more) of the following symptoms of hyperactivity-impulsivity have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level:

Hyperactivity
   (a) often fidgets with hands or feet or squirms in seat
   (b) often leaves seat in classroom or in other situations in which remaining seated is expected
   (c) often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be linked to subjective feelings of restlessness)
   (d) often has difficulty playing or engaging in leisure activities quietly
   (e) is often “on the go” or often acts as if “driven by a motor”
   (f) often talks excessively

Impulsivity
   (g) often blurts out answers before questions have been completed
   (h) often has difficulty awaiting turn
   (i) often interrupts or intrudes on others

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 years

C. Some impairment from the symptoms is present in 2 or more settings (eg, 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 a course of a pervasive developmental disorder, schizophrenia, or other psychotic disorder and are not better accounted for by another mental disorder (eg, mood disorder, anxiety disorder, dissociative disorder, or a personality disorder)


document the degree of impairment in the classroom. It is helpful to have the teacher complete an ADHD-specific behavior checklist and to get narrative information about the child’s classroom behavior, learning patterns, degree of functional impairment, and which classroom interventions are helpful. Involving both families and the educational system during the time of diagnosis can encourage partnership in developing treatment strategies to aid the child.

FURTHER ASSESSMENT

The physician asks the patient’s mother to complete an ADHD symptom checklist and to have the boy’s teacher complete one as well. The physician obtains written permission to talk with the patient’s teacher about his difficulties in school. He meets with the boy alone. The patient admits that he is in trouble at home and school but is largely unaware of his role in his problems. The physician asks the mother to bring copies of her son’s old report cards to the next appointment.

• Which rating scale should be used?

Many rating scales exist to evaluate a variety of psychiatric disorders in children. Two main types of rating scales are often used. The first is the global nonspecific questionnaire, which is used to identify a variety of symptom clusters in children. The most commonly used scale in research and clinical settings is the Child Behavior Checklist (CBCL). This test generates a variety of symptom subscales and is available for several informants. The wide scope of this scale makes it useful for identifying a differential diagnosis and disorders comorbid with ADHD. By itself, however, it is not a very strong measure of ADHD symptoms and is not helpful for repeated administration to monitor treatment. For this reason, global scales are not recommended by the American Association of Pediatrics (AAP) for use in the diagnosis of ADHD because they lack specificity in distinguishing children with ADHD from children without it. The AAP does recommend the use of ADHD-specific screening questionnaires. There are a variety of scales in clinical use (Table 2). When selecting a rating scale, it is important to choose one that is easy to administer, has parent and teacher versions, has strong psychometric properties, and has a normative base. Rating scales are commonly used initially to aid in the diagnosis of ADHD and during follow-up to help monitor the patient’s response to treatment. Two recent studies demonstrate that health-related quality of life (HRQL) measures may have a place in evaluating efficacy of treatment, as responses to the Child Health Questionnaire indicate that symptom severity directly correlates with psychosocial HRQL. It is
important to keep in mind that rating scales alone are not a basis for making a diagnosis of ADHD. It is possible for a parent or a teacher who strongly believes that a child does or does not have the disorder to be biased when completing the scale. They are, however, a useful tool in conjunction with a complete history and physical examination for making the diagnosis.

**FOLLOW-UP**

The physician speaks with the patient’s teacher, who reports that he is very disruptive in class, much more so than his peers. He is unable to sit in his chair for longer than 10 minutes without getting up to move around the classroom. She feels that his hyperactivity and low attention span are making it difficult for him to acquire improved reading skills. She does report that statewide testing indicated that he was performing as expected for a first-grader.

The patient and his mother return in 2 weeks with the completed rating scales. On the scale, the teacher endorsed 7 of 9 inattentive symptoms and 8 of 9 hyperactive/impulsive symptoms. There were no indications of any significant mood or defiant symptoms. The scale showed significant academic impairment with difficulty maintaining focus to acquire new academic skills. The parent rating scale also showed multiple

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**Table 2. Attention-Deficit/Hyperactivity Disorder Rating Scales**

<table>
<thead>
<tr>
<th>Rating Scale (Ages)</th>
<th>Versions</th>
<th>Reliability and Validity Data</th>
<th>Comments</th>
<th>Reference (Publisher)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connors Rating Scale-Revised (CRS-S) (3–17 yr)</td>
<td>Parent Teacher Adolescent self-report</td>
<td>Good to excellent</td>
<td>Evaluates several subscales: cognitive problems/inattention; hyperactivity, oppositional; anxious-shy; perfectionism; social problems; psychosomatic</td>
<td>Connors, 1997 (Multi-Health Systems)</td>
</tr>
<tr>
<td>IOWA Conners (6–12 yr)</td>
<td>Teacher Parent Adolescent</td>
<td>Moderate for teacher No data for parent or adolescent versions</td>
<td>Older scale; continues to be widely used Can overweight minority youth Short administration time; good for multiple administrations</td>
<td>Pelham et al, 1989 (Loney &amp; Milich)</td>
</tr>
<tr>
<td>SNAP-IV (5–11 yr)</td>
<td>Parent Teacher</td>
<td>No published psychometric properties and limited normative data</td>
<td>Used widely in research</td>
<td>Swanson, 1992 (<a href="http://www.ADHD.net">www.ADHD.net</a>)</td>
</tr>
<tr>
<td>SKAMP (7–12 yr)</td>
<td>Teacher</td>
<td>No published psychometric properties and limited normative data</td>
<td>Brief classroom rating scale (included in SNAP-IV) Very specific to ADHD</td>
<td>Wigal et al, 1998 (<a href="http://www.ADHD.net">www.ADHD.net</a>)</td>
</tr>
<tr>
<td>ADHD RS-IV (5–18 yr)</td>
<td>Teacher Parent</td>
<td>Very good to excellent DSM-IV-based Short administration time Little normative data for preschoolers Suboptimal sensitivity and specificity</td>
<td>DuPaul et al, 1998 (Guilford Press)</td>
<td></td>
</tr>
<tr>
<td>Vanderbilt ADHD rating scale (VADRS) (6–12 yr)</td>
<td>Teacher Parent Full version: ADHD + symptoms from other disorders Short version: ADHD</td>
<td>Good to excellent DSM-IV-based New scale—only limited normative data available</td>
<td>Wolraich, 2003 (<a href="http://www.nichq.org">www.nichq.org</a>)</td>
<td></td>
</tr>
<tr>
<td>ADHD-SRS (4–18 yr)</td>
<td>Teacher Parent</td>
<td>Excellent Long administration time Limited use for repeat administration Good for finding ADHD subtypes</td>
<td>Holland et al, 2001 (Wide Range)</td>
<td></td>
</tr>
<tr>
<td>ACTeRS (5–13 yr)</td>
<td>Teacher Parent Self-report</td>
<td>Excellent (teacher) Good (parent) Older scale Unclear normative base Quick to administer and score</td>
<td>Ullman et al, 2000 (Metritech)</td>
<td></td>
</tr>
</tbody>
</table>

ODD = oppositional defiant disorder.
inattentive and hyperactive/impulsive symptoms as well as impairment in social and family functioning.

• **Why should the diagnosis of ADHD be considered in this patient?**

The description of this patient’s symptoms by his parent and teacher is consistent with childhood ADHD. He has significant difficulty sustaining focused attention on classroom tasks as well as on play activities and chore completion at home. He also has multiple hyperactive and impulsive symptoms. The description of his symptoms appears out of the normal developmental expectation for a 7-year-old boy, and there is clear evidence of impairment in both the patient’s ability to function as expected in school and in the home and social environments.

• **Is there a co-occurring psychiatric disorder in this patient?**

Up to two thirds of children with ADHD have a comorbid psychiatric disorder. The most common disorders are ODD (50% of ADHD patients), conduct disorder (30%-50%), mood disorders (20%-25%), and anxiety disorders (20%-25%). Adolescents frequently develop substance abuse and dependence disorders. Learning disorders can be seen in 10% to 25% of children with ADHD, depending on the criteria used to identify the learning problem. Bipolar disorder can be especially difficult to distinguish from ADHD in young children. Children with bipolar disorder usually have clear mood impairments, including elation, grandiosity, severe irritability and anger, a decreased need for sleep, hypersexuality, and racing thoughts. An Icelandic study revealed that children with ADHD, primarily inattentive type, had unprovoked seizures about 2.5 times more often than controls, implicating a connection between ADHD and epilepsy. Children with several disorders are more likely to be seen in a mental health center than be treated by primary care providers.

In this patient, the mother and teacher do not report any significant difficulty with defiance or aggression, which is commonly seen in ODD. The screening scales do not indicate any significant anxious or affective symptoms. There is a possibility that the patient also could have a learning disorder. It can be difficult to identify some learning disorders in children at this age. Because the patient is performing at his grade level, a learning disorder can be ruled out for now.

• **What are initial steps of clinical management?**

**FAMILY EDUCATION**

Management of ADHD begins with educating the patient and family about the disorder. Without an understanding of the disorder, families can view a child’s impulsivity and hyperactivity as misbehavior and become harsh and blaming in their discipline strategies. Examination of a community sample of children with ADHD found negative parental practices to be predictive of persisting ODD. By helping families understand that some of the behaviors are not their child’s fault, the clinician can get them past blaming the child and on to helping.

Education of families about ADHD should include an explanation of the symptoms of the disorder and how it can affect learning, behavior, social skills, and family function. Self-esteem can be decreased in ADHD children by the common poor school performance and frequent negative interactions with adults and peers caused by their impulsive behaviors. The etiology of the disorder including the heritability needs to be discussed. Various treatment options need to be reviewed, including medication effects as well as basic principles of behavior management. It is helpful to give families information about the expected course and prognostic features of the illness. Families also need information on how to advocate for their child in the school setting, work with teachers, and what their child’s legal rights are within the public school system. Some children with ADHD benefit from the development of an individual education plan.

Family members may hold misconceptions about ADHD, and it is important to dispel them. ADHD does not stop at puberty, nor do the medications stop working then. Stimulant medications do not cause drug abuse and do not work paradoxically. Families frequently believe that sugar makes a child more hyperactive, however studies have failed to show that this is the case.

**GENERATING THE TREATMENT PLAN**

Once the patient and family have a more complete understanding of ADHD, it is important to identify areas of dysfunction that need improvement. A treatment plan can be generated to improve multiple areas. Once problem areas are identified, a comprehensive treatment plan can be developed with the family. Examples of target outcomes are

• Improve relationships with parents, siblings, and peers
• Improve academic performance
• Increase independence in self-care or homework completion
• Increase self-esteem
• Decrease disruptive behaviors
• Decrease unsafe community behaviors (eg, running into traffic while crossing the street or riding a bicycle)
MEDICATION MANAGEMENT

Stimulants

Stimulants, first shown to be effective in treating disruptive behavior in 1937, have been used safely in children for many years and are the first-line agents for treating ADHD. Numerous studies have shown them to be effective in significantly improving ADHD symptoms. The Multimodal Treatment Study (MTA) study followed 579 children over 14 months and showed that medication management was superior to behavioral treatment alone and to community treatment in reducing ADHD symptoms. Released in 1998, the MTA was a landmark study because it was the first large long-term study showing that improvement in ADHD symptoms continues over a long period. It divided children into 3 groups: medication management only, combined medication management and behavioral therapy, and behavioral therapy alone. The control group in the study received community treatment, and many of those children were on stimulant medication. The study found that there was little improvement gained by behavioral treatment, and it also showed that current community treatments were not aggressive enough to make significant improvements in ADHD symptoms. The medication group had higher doses of stimulants (38 mg versus 22 mg of methylphenidate) and more frequent doses (3 times daily versus twice daily) than the community treatment group. The study also highlighted the difficulty in completely eliminating ADHD symptoms. Only 38% of the medically managed children in the study had ADHD symptom scores in the normal range at the end of the study. There are 2 main classes of stimulant medications: methylphenidate-based (Ritalin and Concerta) and dextroamphetamine-based (Dexedrine and Adderall). Stimulants work by blocking dopamine transportation in the striatal areas of the brain. This blockade increases the level of dopamine at the synapse and reduces the behavioral problems seen in ADHD. Long-acting and extended-release formulations provide the advantage of once-daily dosing so that children do not have to take the medication in school. With concerns about possible abuse of stimulant medications, the extended-release Concerta capsule is also advantageous in being tamper-resistant. Concerta is well tolerated, and in one study that examined improvement of driving performance in teenagers with ADHD it was shown to be more effective than shorter-acting stimulants. This latter result is likely to apply to most of the long-acting formulations. Other methylphenidate-based medications include Ritalin LA and Metadate CD. Ritalin LA may have a better clinical response in the first 4 hours after administration than Concerta. This same effect was shown when Metadate CD was compared with Concerta, but the latter drug provided longer lasting effects into early evening hours. Dexedrine Spansules are an extended-release form of amphetamine-based stimulant that demonstrated efficacy when compared with immediate-release methylphenidate, extended-release methylphenidate, and pemoline. However, teacher ratings in the morning were lower than for immediate-release forms. Adderall XR was shown to be efficacious in a randomized, double-blind, placebo-controlled, parallel-group study in which parents and teachers noted improvements in afternoon and late afternoon behavior. However, use of Adderall XR may decrease with the advent of a new U.S. Food and Drug Administration (FDA) warning about sudden death associated with this medication. There were a total of 12 cases associated with the drug, 5 of which occurred in patients with underlying structural heart defects; other patients had various medical problems and one had toxic levels of amphetamine at the time of death. The FDA notes that the rate of sudden death in children treated with Adderall is likely not greater than the risk of sudden death in the population, but a labeling change indicates that patients with underlying heart defects not be prescribed this drug.

When choosing a stimulant medication, which class is likely to be more beneficial in treating the symptoms of ADHD? Whether a patient responds preferentially to methylphenidate versus dextroamphetamine or vice versa is likely a function of genetics. Studies of mice show that those with a SNAP-25 deletion had hyperactivity that responded better to dextroamphetamine. This class acts by reversing the DA transporter, while methylphenidate blocks the transporter.

Stimulant side effects include decreased appetite, abdominal pain, insomnia, headache, and tics. More rarely they may cause an aggravation reaction (paradoxical worsening of symptoms), hypertension, weight loss, emotional lability, nervousness, or depression. No serious consequences of prolonged use have been found. Side effects are often mild and are usually transient; when problematic, they can be managed by dose reduction or switching to a different agent. Weight loss can frequently be managed by encouraging parents to increase caloric intake and rarely by stopping medication over the summer to allow for weight gain. Often, the consequences of not adequately treating ADHD are far worse than any potential side effects.

Parents frequently worry that long-term stimulant use will cause growth suppression in their children. Several studies have found that children treated with stimulants for long periods attained adult heights statistically equivalent to those of control groups. In addition, there is
often concern that since stimulants are controlled substances with some abuse potential that using them to treat ADHD will cause children to have substance abuse problems later in life. A recent meta-analysis showed that children who were treated with stimulants for ADHD had a lower risk of developing subsequent drug and alcohol use disorders than children with ADHD who did not receive stimulant medication.57

While Pemoline (Cylert) is a stimulant medication that showed efficacy in a recent study for treating ADHD in adolescents with comorbid substance use disorders,52 it is not frequently used because it has been associated with liver failure and death in rare cases and requires monitoring of liver function every 2 weeks.53

When prescribing stimulant medication to children, begin with a low dose and titrate up until the optimal dose is found. The best dose is one with maximal improvement and fewest side effects. Families commonly think that they only need the medication on school days. If the child has significant impairment in social and family functioning, then they will need dosing on weekends and holidays. This often needs to be specifically discussed with families in order to emphasize the importance of improving not only academic performance, but also family and social relationships. If a child does not respond to one stimulant medication, then the other type should be tried.

**Atomoxetine**

Atomoxetine (Strattera), a selective norepinephrine reuptake inhibitor, is the first nonstimulant medication approved by the FDA for ADHD treatment. It has some advantages over the stimulants: it provides coverage throughout the day and is not a schedule II drug, making prescribing easier. The decrease in abuse potential may be explained by the results of a recent rodent study that compared atomoxetine with methylphenidate and found that while both drugs increase dopamine and norepinephrine in the prefrontal cortex, the former drug did not increase dopamine in the striatum or nucleus accumbens.54 Atomoxetine has been found in studies to be better than placebo in decreasing symptoms of ADHD and improving family and social functioning in school-age children.55,56 A randomized, placebo-controlled, double-blind study indicates that the new medication is also effective for ADHD with comorbid ODD in children and adolescents, although a higher dose (1.8 mg/kg/day versus 1.2 mg/kg/day) was required for patients in the comorbid group than for patients who had ADHD without ODD. However, more studies are needed to determine if there is a true dose differential with the presence of comorbidities.57

Atomoxetine does not have stimulant side effects but is associated with gastrointestinal side effects and sedation that can make it difficult to tolerate. In clinical practice, the improvement in ADHD symptoms does not appear to be as robust as that seen with stimulants.59 It can be considered a first-line agent for those patients who object to or cannot tolerate stimulant medications; however, stimulants should remain the first medication choice for most patients. Recently, the FDA issued a warning for the use of atomoxetine after 2 reports of liver failure, one in a teenager and one in an adult. While these patients recovered and no hepatotoxicity was noted in the 6000 patients who participated in clinical trials, the new labeling indicates that there is a risk of severe liver failure. The drug should be discontinued in patients who develop symptoms or laboratory evidence of hepatotoxicity.59

**Antidepressants**

Several antidepressant medications are used to treat ADHD when stimulants cannot be tolerated or alone are not effective in relieving symptoms. Bupropion (Wellbutrin and Wellbutrin SR), a dopamine and norepinephrine reuptake inhibitor, has been shown in controlled studies to be an effective treatment for ADHD.60 A small, double-blind comparison study of bupropion and methylphenidate showed that both drugs produced significant improvement on ADHD symptom scales.61 Since bupropion is generally well tolerated, it is often used as a second-line agent or added to stimulant medications to improve response. Wellbutrin and all other newer antidepressants have recently been given FDA warnings for possible suicide risk in children and adults; close observation by family members and clinicians is advised. Tricyclic antidepressants also have been shown to be effective in treating ADHD in many studies.62 However, tricyclic antidepressants frequently are associated with adverse events, including several reports of sudden death with desipramine treatment. Imipramine and nortriptyline are somewhat better tolerated than the other tricyclics and occasionally are used as second-line agents. A summary of medications used to treat ADHD is found in Table 3.

### BEHAVIORAL TREATMENT

Behavior therapy involves assessing problematic responses and modifying the physical and social environment to change a child’s behavior. There are a variety of interventions, and they are usually implemented by training parents and teachers to use specific techniques to improve behavior. Parent training in behavior therapy and classroom behavior interventions have been found to be effective in successfully improving the behavior of children with ADHD.63 Four main techniques are used.
Positive reinforcement provides rewards or privileges contingent on a child’s performance of appropriate or desired behaviors. Time-out involves removing access to a positive reinforcement contingent on a child exhibiting unwanted behavior. Response cost involves withdrawing privileges or rewards contingent on the performance of problem behavior. A token economy can be implemented, which combines positive reinforcement and response cost. The child earns rewards and privileges if he performs desired behaviors and loses rewards and privileges if he demonstrates undesirable behavior.64

**OTHER INTERVENTIONS**

It might seem intuitive that medication combined with specific psychosocial treatments might produce better improvement of symptoms than pharmacologic therapy alone. In a 2-year study, 103 children who showed response to methylphenidate were randomized to 3 groups: (1) methylphenidate treatment alone; (2) methylphenidate combined with multimodal psychosocial treatment, which included parent training and counseling, academic assistance, psychotherapy, and social skills training; or (3) methylphenidate plus attention control treatment, which included specific aspects of psychosocial intervention. After 12 months, the children were switched to single-blind placebo and methylphenidate reinstituted when clinically indicated. Results showed that significant improvement occurred across all groups and the improvement continued over 2 years for measures of symptom improvement, academic achievement, social functioning, and parenting practices. However, there was no significant advantage conferred to the group who received multimodal psychosocial treatment; similar improvements were observed in both control groups. Based on the results of this long-term study, there is no advantage of psychosocial treatment combined with stimulant treatment over stimulant treatment alone.65–69

Another study makes use of the computer age in a multicenter, randomized, controlled, double-blind trial

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**Table 3. Pharmacologic Agents for Treatment of Attention-Deficit/Hyperactivity Disorder**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Formulations</th>
<th>Recommended Dose</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line medications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>Ritalin</td>
<td>5-, 10-, 20-mg tab</td>
<td>5 mg bid (AM and noon), Max: 60 mg/d</td>
<td>3–5 hr</td>
</tr>
<tr>
<td></td>
<td>Methylin</td>
<td>5-, 10-, 20-mg tab</td>
<td>5 mg bid–tid, max 40 mg/d</td>
<td>4–6 hr</td>
</tr>
<tr>
<td></td>
<td>Focalin</td>
<td>2.5-, 5-, 10-mg tab</td>
<td>5 mg bid–tid, max 40 mg/d</td>
<td>4–6 hr</td>
</tr>
<tr>
<td>Intermediate duration</td>
<td>Ritalin SR</td>
<td>20-mg tab</td>
<td>20–40 mg po qd or bid</td>
<td>3–8 hr</td>
</tr>
<tr>
<td></td>
<td>Metadate ER</td>
<td>10-, 20-mg tab</td>
<td>equivalent to prior short-acting dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methylin ER</td>
<td>10-, 20-mg tab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long duration</td>
<td>Concerta</td>
<td>18-, 27-, 36-, 54-mg tab</td>
<td>1 q AM, max 72 mg/d</td>
<td>12 hr</td>
</tr>
<tr>
<td></td>
<td>Metadate CD</td>
<td>20-mg cap (6 mg IR, 14 mg ER)</td>
<td>1 q AM, max 60 mg/d</td>
<td>8 hr</td>
</tr>
<tr>
<td></td>
<td>Ritalin LA</td>
<td>20-, 30-, 40-mg cap (½ IR, ½ ER)</td>
<td>1 q AM, max 60 mg/d</td>
<td>8 hr</td>
</tr>
<tr>
<td>Amphetamine/ dextroamphetamine</td>
<td>Dexamphetamine</td>
<td>5-mg tab</td>
<td>5 mg bid–tid, max 40 mg/d</td>
<td>4–6 hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5-, 10-mg tab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate duration</td>
<td>Dexamphetamine Spansule</td>
<td>5-, 10-, 15-mg cap</td>
<td>5–10 mg qd–bid, max 40 mg/d</td>
<td>6–8 hr</td>
</tr>
<tr>
<td></td>
<td>Adderal</td>
<td>5-, 7.5-, 10-, 12.5-, 15-, 20-, 30-mg tab</td>
<td>5–10 mg qd–bid, max 40 mg/d</td>
<td>6–8 hr</td>
</tr>
<tr>
<td>Long duration</td>
<td>Adderal XR</td>
<td>5-, 10-, 15-, 20-, 25-, 30-mg cap</td>
<td>10 mg qd, max 30 mg po qd</td>
<td>10–12 hr</td>
</tr>
<tr>
<td>Atomoxetine</td>
<td>Strattera</td>
<td>10-, 18-, 25-, 40-, 60-mg cap</td>
<td>Initial: 0.5 mg/kg q AM or bid, increase after 3 days to 1.2 mg/kg q AM or bid</td>
<td>24+ hr</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Max: 1.4 mg/kg/d or 100 mg/d</td>
<td></td>
</tr>
<tr>
<td><strong>Second-line medications</strong></td>
<td>Wellbutrin</td>
<td>75- and 100-mg tab</td>
<td>100–150 mg qd–tid</td>
<td>6–8 hr</td>
</tr>
<tr>
<td></td>
<td>Wellbutrin SR</td>
<td>100- and 150-mg tab</td>
<td>100–200 mg qd–bid</td>
<td>12 hr</td>
</tr>
<tr>
<td></td>
<td>Wellbutrin XL</td>
<td>150- and 300-mg cap</td>
<td>150–450 mg qd</td>
<td>24 hr</td>
</tr>
</tbody>
</table>

ER = extended release; IR = immediate release.
to determine if practice of working memory tasks can improve working memory in children with ADHD. A span-board task that was not practiced during the treatment period was used to test the effect of the computerized training on children who were not treated with stimulant medication. They were randomized to either complete a treatment computer training program specifically designed to improve working memory or complete a comparison program. The span-board task, designed to test visual working memory, showed improvement for the treatment group both postintervention and at 3-month follow-up. This improvement implies that training can ultimately improve performance of executive function, such as reasoning and control of attention.

**TREATMENT IN THIS PATIENT**

The patient was prescribed a long-acting stimulant medication at the low initial dose to be taken once each morning. Over several monthly visits, with follow-up teacher and parent rating scales completed on alternating months, his dose was increased and was one dose below the maximum dose after 4 months. Once the patient was at the optimal dosage, both parents and teacher reported minimal difficulty with attention and hyperactivity. He had some appetite suppression initially that resolved without any intervention other than to encourage eating at mealtimes. Over several months of follow-up, he began to gain weight and height as expected on his growth curve. The family was able to advocate for educational interventions within the school system, and the patient was placed on an individualized education plan. They found that several of the ADHD Web sites offered helpful advice for handling problem behaviors.

After 3 years of treatment and occasional dose increases, the family found that the patient’s aggression with friends and refusal to comply with parental requests were problematic. They were referred to a mental health professional, and the parents received training in dealing with the behavioral difficulties posed by ADHD while the patient participated in an ADHD social skills group. The parents determined that they had been too lenient in their discipline strategies and began to employ the behavioral therapy techniques, which helped reduce their child’s defiant behaviors. The patient found that the social skills training helped him to get along better with his peers, and he continued to be a successful student and developed more meaningful peer relationships.

**REFERENCES**

Attention-Deficit/Hyperactivity Disorder in Children

25:166–74.


