Attention-Deficit/Hyperactivity Disorder

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a common neurobiologic disorder characterized by developmentally inappropriate levels of inattention, hyperactivity, and impulsivity. ADHD also is one of the most prevalent chronic health conditions affecting school-age children. Consequently, physicians frequently are asked to evaluate children for a possible diagnosis of ADHD. The importance of an appropriate and timely diagnosis is based on the knowledge that children who have ADHD may experience difficulty in social, emotional, and academic domains and that treatment can improve outcomes for these children.

Prevalence

ADHD is a behavioral disorder, making it difficult to quantify. Epidemiologic studies indicate that at least 3% of children in the United States are affected by ADHD, with usual quoted rates of 5% and 8%. (1) Prevalence rates for ADHD vary, depending on the patient sample, geography, and diagnostic criteria (Table 1). The diagnosis is reported 2.5 times more frequently in boys than in girls, with 9.2% of males and 2.9% of females found to have behaviors that are consistent with ADHD. ADHD is considered a lifelong condition. Among adolescents who receive ADHD diagnoses as children, 60% to 80% continue to meet criteria for ADHD during their teenage years and adulthood.

Prevalence rates for ADHD vary by age. Studies indicate that school-age children are more likely to be diagnosed compared with preschool-age children and adolescents. Approximately 50% of children who receive the diagnosis are treated with medication. According to a 2003 National Survey of Children's Health, 56.3% of children who had reported ADHD were being treated with medication at the time of the survey, and school-age children were most likely to be receiving medication for ADHD. (2)

Studies have not demonstrated a consistent association among ADHD prevalence and race, ethnicity, or socioeconomic status. However, environmental and biologic factors may increase the risk of ADHD. Environmental factors include early lead exposure and prenatal exposure to cigarette smoking and alcohol. Biologic factors such as low birthweight, prematurity, and intrauterine growth restriction also increase the risk for ADHD.

Causes

Research in the fields of neurobiology, genetics, and neuropsychology support a biologic basis for ADHD. Many studies show an association between ADHD and biologic systems that are believed to control attention and regulate inhibition. However, no single cause of ADHD has been identified

Neuroimaging studies have shown structural and functional differences in areas of the brains in patients who have ADHD compared with patients who have no ADHD. Certain regions of the brain, rich in dopaminergic and noradrenergic pathways and associated with executive function, seem to be particularly affected, including the prefrontal cortex, striatum, and cerebellum. Functional magnetic resonance imaging (MRI) studies suggest that these particular regions of the brain are less activated in children who have ADHD compared with those of age-matched controls during activities that measure executive function, a cognitive process of the frontal lobe that is used to solve problems or achieve a goal. Other studies, using brain MRI, have found reductions in prefrontal, frontal, and hemispheric volumes in individuals who have ADHD compared with controls. The clinical significance of these differences is not clear.

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Table 1. Diagnostic Criteria for Attention-Deficit/Hyperactivity Disorder

A. Either 1 or 2

1. Six or more of the following symptoms of inattention have persisted for at least 6 months to a degree that is maladaptive and inconsistent with developmental level

Inattention

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

2. Six 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

1. Often fidgets with hands or feet or squirms in seat
2. Often leaves seat in classroom or in other situations in which remaining seated is expected
3. 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)
4. Often has difficulty quietly playing or engaging in leisure activities
5. Often is "on the go" or acts as if "driven by a motor"
6. Often talks excessively

Impulsivity

7. Often blurts out answers before the questions have been completed
8. Often has difficulty awaiting turn
9. Often interrupts or intrudes on others (eg, butts into conversations or games)

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

C. Some impairment from the symptoms is present in two or more settings (eg, at school or 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 psychotic disorder and are not better accounted for by another mental disorder (eg, mood disorder, anxiety disorder, dissociative disorder, or personality disorder)

Several studies support the hypothesis that ADHD is associated with deficits in executive functioning. Studies based on results from neuropsychological tests of executive function in children who have ADHD showed that these children performed poorly compared with age-matched controls on specific tasks. Although these results improve understanding of the cognitive problems that some children who have ADHD may face, the results do not provide adequate evidence to conclude that problems with executive function are specific to ADHD. However, executive function deficits may be a comorbid problem among children who have ADHD. Tests of executive function, such as set shifting, working memory, or processing speed, and other neuropsychological tests, such as continuous performance testing, should not be used alone to diagnose ADHD. (3)

Genetic studies suggest that ADHD is an inherited disorder. ADHD is more likely if a parent or sibling has been diagnosed with the disorder. This conclusion is supported by the high concordance for ADHD in identical twins as well as by family studies. Multiple genes contribute to the ADHD phenotype, including those related to monoaminergic (dopaminergic, serotonergic, and noradrenergic) neurotransmission. These genes include dopamine receptor genes (*DRD4* and *DRD5*) and a dopamine transporter gene (*DAT1*). The basis for these studies emerged from evidence indicating that these neurotransmitters are involved in the modulation of at-

tention and behavioral regulation in the frontal cortex. Despite the increased prevalence in male children, no study has shown that ADHD is attributable to an X-linked effect.

Defining ADHD

ADHD is defined as a mental health disorder in the *Diagnostic and Statistical Manual 4th Edition* (DSM IV). (4) Over the years, the diagnostic criteria have been revised as clinical impressions of what constitutes this disorder have shifted. The most current definition of ADHD is listed under DSM IV criteria as "a persistent pattern of inattention and/or hyperactivity-impulsivity that is more frequent and severe than is typically observed in individuals of comparable levels of development." The DSM IV criteria were developed by a committee and were based on a review of the literature and an analysis of field trials to determine whether the symptoms of ADHD had diagnostic utility. This effort led to the development of the two broad categories of symptoms (inattention and hyperactivity/impulsivity) and the distinction of three subtypes of ADHD (predominantly inattentive, predominantly hyperactive/impulsive, and combined type) (Table 1). To meet criteria for the predominantly inattentive subtype, the child must exhibit six of nine symptoms from A1. To meet criteria for the predominantly hyperactive subtype, the child must exhibit six of nine symptoms from category A2. To meet criteria for the combined type, the child must exhibit six of nine symptoms from both categories.

Diagnosing ADHD

Overview

ADHD is a behavioral disorder. Diagnosis requires a comprehensive clinical evaluation based on identifying children who have the core symptoms of inattention, hyperactivity, and impulsivity and whose behavior is sufficiently severe and persistent to cause functional impairment. No single test is available to establish the diagnosis. Although many children may be inattentive, hyperactive, or impulsive, the level of severity and degree of functional impairment, as well as considerations of what else might be causing the symptoms, determine which children meet the diagnosis and are treated for ADHD.

To assist clinicians with the accurate identification of children who have ADHD, the American Academy of Pediatrics (AAP) published a clinical practice guideline in 2000. (5) This guideline specifically urges primary care physicians to initiate an evaluation for ADHD in "any child, ages 6 to 12, who presents with the core symptoms of ADHD, behavior problems or academic difficulties." In addition, the guideline specifies that:

1. The child's symptoms meet the DSM IV criteria for ADHD.
2. Information be collected from the parents or caregivers regarding the core symptoms of ADHD, the age of onset, the duration of symptoms, and the degree of functional impairment.
3. Information be obtained from another source such as the classroom teacher regarding the core symptoms of ADHD, the duration of symptoms, and the degree of impairment.
4. An assessment of potential coexisting conditions, such as mood disorders or learning disabilities, be performed.

Initiating an Evaluation

The initial evaluation for suspected ADHD may be prompted by a variety of clinical circumstances. A clinician may become concerned about ADHD during a routine health supervision visit after screening for behavior and emotional problems. More frequently, parents, teachers, caregivers, or other professionals may raise concerns independent of any health-care screening effort. For example, parents may be concerned about their child's declining academic performance, relationship difficulties with peers or family members, or symptoms of emotional problems.

Once a concern is identified, an initial screening begins by obtaining a description of the child's behavior and its impact on his or her ability to function in school, at home, and with peers. During the screening process, it should be determined if evidence is sufficient to proceed with an additional evaluation for ADHD. Useful questions at this point should address the child's academic performance, homework completion, behavioral or mood problems, and peer relationships.

While gathering information, the clinician should be aware that the presenting symptoms of ADHD vary with the age and developmental level of the child. For example, during the preschool years, many children are inattentive, hyperactive, or impulsive. It may be difficult to distinguish age-appropriate levels of physical activity and short attention span from those activity levels and attention spans in children who have ADHD. Although the AAP guideline does not include specific recommendations regarding the diagnosis of ADHD in this population, studies show that preschool-age children may have significant attention or behavioral problems consistent with a diagnosis of ADHD. However, among preschool-age children who receive the diagnosis of ADHD, fewer

than 50% continue to have the diagnosis during childhood. The degree, duration, and pervasiveness of ADHD symptoms help to distinguish those children who are most likely to develop a persistent pattern of behavior that is consistent with ADHD.

As children enter elementary school, activity levels decline and children are expected to sustain attention for longer periods of time, to complete tasks independently, and to work cooperatively with their peers. At this age, children typically are able to focus for longer periods of time but may be impulsive at times. Teachers and parents of children who have underlying ADHD may express concerns about the child's safety or his or her ability to remain focused in class or to follow school routines.

During adolescence, demands are greater for organizational skills, time management, and the mastering of large amounts of material. Some adolescents who have ADHD, especially the predominately inattentive type, may not receive a diagnosis until middle school or high school. If there are not signs of significant impairment in functioning, a diagnosis of ADHD cannot be made. However, a diagnosis of ADHD still should be considered if an undiagnosed adolescent manifesting previous symptoms becomes more disruptive in class, exhibits increased academic problems, engages in increased risk-taking behavior, or becomes oppositional as the academic and maturational challenges increase.

Confirming the Symptoms

If the history indicates that a child's behavior is contributing to significant impairment in more than one setting, the clinician may proceed with the diagnostic process. Specific information about the child's symptoms to determine if they meet DSM IV criteria for ADHD must be obtained and whether another cause might better explain the symptoms must be determined. Both the parent and child should be interviewed to determine information about the child's behavior as well as the onset, duration, and severity of symptoms and the context in which the symptoms occur. For example, the clinician may inquire about the child's behavior in various situations: completing homework assignments and long-term school projects, getting ready for school in the morning, relating to peers, sitting in class, or following instructions. In cases where the presenting symptoms of inattention, hyperactivity, or impulsivity do not meet criteria for ADHD but warrant additional behavioral interventions or parent education, the clinician can use the *Diagnostic and Statistical Manual for Primary Care* (DSM-PC) (6) to document the child's behavior in the medical record and to develop an intervention plan.

The medical record should contain specific descriptions of the child's symptoms and not simply state that the child is inattentive, hyperactive, or impulsive. For example, the description of a hyperactive middle school child may indicate that the child leaves his seat during class, runs out of the classroom, fidgets endlessly, or has difficulty sitting still during any activity that requires concentration.

Because the DSM-IV symptoms were not selected scientifically and because there is substantial overlap among the symptoms, it is harder to establish a rating scale or a scientific scoring to determine whether a specific child has ADHD. Therefore, ADHD-specific rating scales are not diagnostic. However, they may be used to gather information about the child's behaviors from the parent, teacher, or both. In general, these rating scales assess the core symptoms of ADHD, as specified in the DSM IV, and they are relatively easy to administer (Table 2). The strength of the rating scales lies in their link to DSM IV symptoms. Rating scales probably are most useful in documenting whether the rater sees the core symptoms as being present for a specific child compared with his or her same-age peers. Broad-band rating scales that are not ADHD-specific have not been shown to provide sufficient evidence to support their use in the assessment of ADHD. (5)(16)

When choosing a rating scale, it is important to realize their limitations. Two different clinical situations illustrate this problem. First, although most of the ADHD-specific rating scales demonstrate good concurrent validity with other established instruments that are used to measure similar behaviors, they may not be good measures of developmental variations in the expression of ADHD. Second, when a child's behaviors do not conform to DSM IV criteria, such as ADHD complicated by oppositional behaviors, the diagnosis may be missed if the clinician only uses the DSM IV criteria to establish a diagnosis of ADHD.

The clinician also should recognize that ADHD-specific rating scales differ in their normative data. For example, normative data for the Connors Scales and the Attention Deficit Disorder Evaluation Scale (ADDES-3) were formulated based on discrete age ranges (eg, comparing ages 3 to 5, 6 to 8); other scales, such as the ADHD-Symptoms Rating Scale (ADHD-SRS), established normative data based on broader age ranges (eg, 5 to 12 years, 13 to 18 years). Only the Connors Scales have normative data for preschool-age children. Norma-

tive data also may differ by race, sex, and geographic area. Therefore, when using a rating scale, it may be difficult to interpret the results if the clinician's particular patient sample is not represented in the scale's normative data.

Rating scales also may be used to measure behavioral changes that occur over time or in response to treatment. However, few studies have been published that describe their diagnostic utility in this context. When using a rating scale for these purposes, it is best to select one that has sufficient test-retest reliability and good sensitivity to treatment effects.

Many of the ADHD rating scales also provide screening questions for comorbid conditions. In many cases, the validity and psychometric properties of these subscales have not been determined.

In summary, ADHD-specific rating scales are useful but must be interpreted within the clinical context of the child being evaluated. Rating scales should be used to supplement information obtained from a clinical history as well as to assess the functional consequences of the behaviors. Despite the benefits of using rating scales, their scores alone do not establish a diagnosis. Clinical judgment is needed to integrate the results of these scales into the clinical assessment.

Differential Diagnosis and Coexisting Conditions

The evaluation of a child for ADHD should include careful consideration of other possible explanations for the symptoms as well as an assessment of possible coexisting conditions and disorders (Table 3). It is important to consider whether family stressors (including domestic violence), lack of sleep (from organic disorders such as sleep apnea or nonorganic conditions such as poor sleep hygiene), sensory impairments, a seizure disorder, inappropriate school placement, or unrealistic expectations is the cause of the symptoms. In addition, psychiatric disorders such as autism, anxiety problems, mood disorders, specific learning disabilities, or intellectual disability may present with symptoms that mimic ADHD. Skillful interviewing may help determine whether another disorder is the sole explanation for the symptoms or represents a coexisting disorder.

Studies show that as many as 67% of children who have ADHD may have a coexisting condition such as a psychiatric problem, learning disorder, or social immaturity. The more common comorbid psychiatric conditions that have been described include oppositional defiant disorder (prevalence of 35%), conduct disorder (preva-

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

Scale	Normative Data (ages)	Benefits	Limitations
Conners-3 Conners-EC (Early Childhood) Conners (7,8)	6 to 18 years 2 to 6 years	Adolescent self-report available	Multiple versions available; may be confusing
Swanson, Nolan, and Pelham IV Questionnaire (SNAP IV) Swanson 1992 (9)	5 to 11 years	Scoring available on the Internet	Limited normative data
ADHD Rating Scale IV (ADHD RS IV) DuPaul et al 1998 (10)	5 to 18 years		Only asks about DSM-IV ADHD symptoms
Vanderbilt ADHD Rating Scale (VARS) Wolraich 2003 (11)	Elementary school	Includes rating of impairment; asks about comorbid symptoms	No normative data on adolescents
ADHD Symptoms Rating Scale (ADHD-SRS) Holland et al 2001 (12)	5 to 18 years		Lengthy
Attention Deficit Disorder Evaluation Scale-3rd Edition (ADDES-3) McCarney 2004 (13)(14)	4 to 18 years		Lengthy
ACTeRS-2nd Edition Ullman et al 2000 (15)	Kindergarten to 8th grade for teacher version	Adolescent self-report available	Normative data on parent and adolescent version not published

Each scale has a parent and teacher version except the SNAP IV.

Table 3. Coexisting Disorders and Differential Diagnosis of Attention-Deficit/Hyperactivity Disorder

Developmental Disorders
Language disorder
Learning disability
Intellectual disability
Autism spectrum disorders
Developmental coordination disorder
Medical Disorders
Lead intoxication
Anemia
Medication adverse effects
Seizure disorder
Substance abuse
Sensory deficits
Prematurity
Fetal alcohol syndrome
Tourette syndrome
Sleep apnea
Genetic Disorders
Klinefelter syndrome
Fragile X syndrome
Turner syndrome
22q11.2 deletion syndrome
Williams syndrome
Neurofibromatosis I
Inborn errors of metabolism
Psychiatric Disorders
Adjustment disorder
Anxiety disorder
Attachment disorder
Mood disorder
Oppositional defiant disorder
Posttraumatic stress disorder

Adapted from Lock TM, Worley KA, Wolraich ML. Attention deficit/hyperactivity disorder. In: Wolraich ML, Drotar DD, Dworkin PH, Perrin EC, eds. *Developmental-Behavioral Pediatrics: Evidence and Practice*. Philadelphia, Pa: Mosby, Inc; 2008: 579–601.

lence of 30%), anxiety disorder (prevalence of 25%), and mood disorder (prevalence of ~18%). (4) These coexisting conditions also need to be addressed. Although some of these coexisting conditions may improve as the ADHD is treated, most require separate intervention.

Depending on the specific definition and treatment setting, 12% to 60% of children who have ADHD may have a coexisting learning or language problem. The most common learning disorder is a written language disorder. Because most children who have ADHD experience academic underachievement, it is important to distinguish whether a learning disability also is present. The patient's history may provide clues to the underlying reasons for academic problems. For example, if a child's ADHD symptoms are more likely to occur during a particular activity or setting, a learning disorder may be present. Psychological testing combined with achievement testing may help to identify a learning disorder. Learning problems are more likely to occur in children who have the predominantly inattentive or combined subtypes of ADHD.

The differential diagnosis of ADHD also includes medical conditions, genetic disorders, neurologic disorders, and developmental disorders that may contribute to a child's symptoms of inattention, impulsivity, or hyperactivity. Although the DSM IV criteria for ADHD specifically exclude developmental disorders such as intellectual disability and pervasive developmental disorders such as autism, children who have these disorders may present with symptoms of inattention, hyperactivity, or impulsivity that are consistent with ADHD and treatable according to accepted standards for ADHD treatment.

Treatment

In 2001, after extensive review of the scientific literature, the AAP published an evidence-based clinical practice guideline for the treatment of the school-age child who has ADHD. (17) A key study considered in developing this guideline was the National Institute of Mental Health Collaborative multi-site multimodal treatment study of children with attention deficit/hyperactivity disorder (MTA study). (18) In the MTA study, children were randomized to four groups: medication treatment alone (these children also had monthly 30-minute follow-up appointments, during which some brief counseling was included), intensive behavioral treatment alone, a combination of medication management and behavioral treatment, and community treatment as the control group.

The MTA study showed that pharmacologic intervention for ADHD was more effective than behavioral treatment alone. Combination treatment was no better than medication alone, except when the children studied also had a comorbid anxiety or oppositional defiant disorder. When those comorbid conditions were present, combination treatment was more effective than medication alone. Satisfaction with treatment reported by teachers and parents was highest in the combination treatment group.

The AAP guideline includes five recommendations

regarding treatment of ADHD: 1) Approach and treat ADHD as a chronic health condition, 2) Collaborate with partners in designing and evaluating treatment plans and outcomes, 3) Provide medication management, 4) Provide periodic systematic follow-up, and 5) Evaluate treatment failure as needed.

Treat ADHD as a Chronic Health Condition

The 2001 AAP practice guideline emphasizes that ADHD is a chronic health condition. This chronic care model, originally designed for adults, was adapted for use in children by the National Initiative for Children's Healthcare Quality. This model emphasizes ongoing parental and child education about ADHD and its treatments. The treatment of ADHD as a chronic care condition involves engaging the family, the child, and professionals in the schools (teachers, nurses, psychologists, counselors) in the assessment and long-term treatment of this disorder.

Collaborate With Partners Regarding Treatment Goals

The primary goal of ADHD treatment is to maximize the child's functioning in the home and school. The clinician's role is to design and implement an individual treatment plan for the child in partnership with the family that sets treatment goals and priorities. The clinician also collaborates with the educational system to address the child's symptoms and monitor the response to medication within the school. The process of developing target outcomes requires input from the parents, teachers, and other professionals involved with the child.

Although some children who have ADHD respond to medication intervention and no longer need special accommodations at school, others may need significant support to participate fully in their educational programs. Thus, school-based interventions become an integral aspect of behavioral treatment and educational support for children who have ADHD.

The Rehabilitation Act of 1973 provides the legal basis for school-based accommodations once a disability such as ADHD is identified. According to Section 504 of the Rehabilitation Act, parents may request accommodations within the regular classroom based on the child's individual needs. Examples of accommodations include preferential seating, modified assignments and homework load (such as dividing longer assignments into shorter manageable parts), use of visual cues and reminders to help children stay on task, and frequent motor breaks from the classroom routine. The clinician may help parents understand the value of these educational accommodations, explain the process of requesting and implementing a 504 plan, and make suggestions regarding the specific accommodations

When children diagnosed as having ADHD need special education services for a comorbid learning disability or because of the functional impact of their ADHD symptoms, parents may request an Individualized Education Plan (IEP) according to the provisions of the Individuals with Disabilities Education Act (IDEA). An IEP also may include counseling and a behavior management program. A yearly review of treatment goals and the child's progress is mandatory under IDEA. A clinician may participate in this process by making recommendations regarding these goals and treatments (Table 4).

The use of a daily report card provides parents and teachers with a communication tool that records a child's progress in achieving treatment goals and provides opportunities for rewards and consequences.

Medication Management

For most children, stimulant medication is highly effective in treating the core symptoms of ADHD. Therefore, initiation of medication often is recommended in the treatment for school-age children who have ADHD. General guidelines for medication management include:

1. Initiate treatment with a stimulant medication from the amphetamine or methylphenidate group. If one stimulant group does not work, switch to the other.

2. Dosing of stimulant medication is not weight-dependent. Start with a low dose and titrate until ADHD symptoms are manageable, maximum dose is reached, or adverse effects prevent additional titration. Generally, the relationship between dose and clinical response is

Table 4. Examples of Treatment Goals

- Improve academic performance: work completion, accuracy, efficiency
- Improve independence in self-care and school work
- Improve relationships with parents, siblings, peers, and teachers
- Decrease frequency of disruptive behavior
- Improve self-control
- Improve self-esteem
- Improve safety in the community; reduce inappropriate risk-taking behavior

Adapted from AAP Clinical Practice Guideline. Treatment of the school-aged child with ADHD. *Pediatrics.* 2001;108:1033–1044.

linear, with a greater reduction in symptoms achieved at higher doses of stimulant medication.

3. Initiation of treatment with an extended-release preparation of medication often is preferred, especially for older children who need medication coverage for extended periods of time (there is no need to start with short-acting medications).

4. Use of parent and teacher ADHD rating scales is helpful during the titration phase and periodically thereafter to determine response to medication and to monitor adverse effects.

5. At each visit, monitor for growth impairment by measuring height and weight; monitor for potential cardiac effects of the medication (such as elevated blood pressure or tachycardia) by measuring blood pressure and pulse.

6. A 1-month follow-up visit is recommended after starting the medication. Additional follow-up visits are based on treatment response but should occur at least twice a year. Treatment of ADHD should continue as long as symptoms remain present and cause impairment.

7. If a child who has ADHD shows full remission of symptoms and normative functioning, behavior therapy may not need to be added to the regimen.

8. Additional laboratory investigation or electrocardiography is not recommended unless clinically indicated. (19)

First-line Agents: Stimulant Medications

Stimulant medications are considered the first line of treatment for ADHD because they are highly efficacious in reducing symptoms. More than 80% of children who have ADHD respond to stimulants (although a few medication trials may be needed before finding the agent that elicits the best response). Two categories of stimulants are available: methylphenidate and amphetamine compounds. Studies indicate that each of these groups of stimulants has equal efficacy. Their primary mode of action is to enhance central nervous system catecholamine action, probably by increasing the availability of dopamine and norepinephrine at the synaptic cleft level in the frontal cortical-striatal circuits that regulate attention, arousal, and impulse control. When converting between dextroamphetamine and methylphenidate products, the equivalent dose of a dextroamphetamine product generally is half that of a methylphenidate product (except for dexmethylphenidate, which has the same dose).

Both categories of stimulant medications are available as short-, intermediate-, and long-acting formulations. The onset of action usually is within 30 minutes but may be longer, especially with methylphenidate hydrochloride or with methylphenidate transdermal. Stimulant medications are classified as category II controlled substances because they have the potential for abuse or dependence. However, multiple studies indicate that children taking stimulants to treat ADHD do not develop dependence or signs of addiction, they do not need escalating doses beyond that expected from their growth, and they do not suffer withdrawal symptoms when they stop taking their stimulant medications. Multiple studies of children taking stimulants to treat their ADHD also suggest that taking such medications decreases, rather than increases, the child's risk for addiction to illicit drugs.

Children who have ADHD and are treated with stimulants show improvement in attention to task and decrease in impulsivity and hyperactivity. Stimulants also may improve parent-child interactions, reduce aggressive behavior, and improve a child's academic productivity and accuracy. The effect on academic performance is less strong.

Stimulants generally are well tolerated. However, appropriate medication management requires interviewing both the parent and child regarding possible adverse effects. The most common adverse effects of stimulants are decreased appetite, abdominal pain, headaches, irritability, and sleep problems. Gastrointestinal effects and headaches may be lessened if the medication is taken with food. Less common adverse effects include weight loss, "rebound" effects, tics, social withdrawal, and affective changes. Rebound refers to temporary worsening of symptoms (irritability, increased activity, or mood swings) when the medication wears off. Administering a low dose of an immediate-release (short-acting) stimulant at this time may be helpful. Social withdrawal, lethargy, or restricted affect may be a result of overdosing. Rare adverse effects include psychotic behavior that may present as hallucinations or mania.

Tics are reported with varying frequency after the start of stimulant medication. Stimulant medication may lower the threshold for the development of tics, but such medications are not believed to "cause" tics. The presence of tics is not a contraindication to stimulant use. The decision to modify drug treatment based on the presence or development of tics should be individualized for each patient. The clinician and the family may consider factors such as the improvement in symptoms versus the impairment caused by the tics when trying to make such a decision.

The effect of stimulants on long-term growth continues to be studied. Short-term use of stimulants (studies

evaluating up to 3 years of treatment) can cause a transient lag in growth, with most growth deficits occurring in the first year. Fewer data are available concerning long-term treatment and its impact on final adult height with long-term stimulant use. (20)

Recent attention has focused on the risk of sudden cardiac death in pediatric patients who are treated with stimulant drugs. After careful consideration of the available data, the AAP published a policy statement in 2008 regarding cardiovascular monitoring and stimulant drugs for ADHD. (19) The statement recommends assessing all children, including those in whom stimulant medication is being considered, using a targeted cardiac history (patient history of previously detected cardiovascular disease, palpitations, syncope, or seizures; family history of sudden death in children or young adults; hypertrophic cardiomyopathy, long QT syndrome) and a physical examination (including a cardiac examination). Routine electrocardiography is not indicated before starting a child on stimulant medication. Special caution is recommended before using stimulant medications in children or adolescents who have pre-existing cardiovascular disease or symptoms suggesting cardiovascular disease. In these cases, consultation with a pediatric cardiologist is recommended.

All children who are prescribed stimulant medications require regular monitoring of pulse and blood pressure. Small elevations in pulse or blood pressure may not be clinically significant. If significant elevations occur, evaluation for an underlying medical problem should be initiated.

Second-line Agents: Nonstimulant Medications

Atomoxetine is considered a second-line drug for the treatment of ADHD because it has been shown to be less effective in treating ADHD symptoms when compared with stimulants. Atomoxetine is a selective inhibitor of the presynaptic norepinephrine transporter in the central nervous system. It increases norepinephrine and dopamine concentrations, especially in the prefrontal cortex. This medication has been approved by the United States Food and Drug Administration (FDA) for treatment of children ages 6 years and older who have ADHD.

Atomoxetine has a longer half-life compared with that of stimulants. Therefore, treatment effects may not be noted for several days and a steady state not be reached for up to 6 weeks. Some data show efficacy in treatment of ADHD with comorbid anxiety disorder. Atomoxetine also may be used in situations where substance abuse is a concern because this medication is not a class II drug.

Most common adverse effects of atomoxetine include decreased appetite, abdominal pain, nausea, and somnolence. Among the less common adverse effects are headaches, fatigue, dyspepsia, vomiting, and diarrhea. Rare cases of hepatitis (reversible) have been related to this medication. Some studies show that tics are less likely to develop with atomoxetine treatment. In 2005, a "black box" warning was added regarding an increased risk for suicidal ideation or suicidal behavior, similar to that found with selective serotonin reuptake inhibitors.

FDA-approved medications for treating ADHD are listed in Table 5. Contraindications to medications for treating ADHD are listed in Table 6. Patient medication guidelines, required by the FDA in 2006 and published by the individual drug manufacturers, can be accessed on the FDA Center for Drug Evaluation and Research web page. (21) These guides inform parents about possible cardiovascular risks, psychiatric effects, and contraindications of the medications.

Second-line agents not approved by the FDA may be used to treat ADHD. These medications include antidepressants (tricyclic antidepressants, bupropion) and alpha-2-adrenergic agonists (clonidine, guanfacine). A review of these medications is beyond the scope of this article.

Nonpharmacologic Interventions

Behavioral Therapy

Behavioral interventions (Table 7) are directed at manipulating the physical and social environment to modify behavior. These interventions can be used in the home and school. Behavior therapy may be recommended as an initial treatment when ADHD symptoms are mild and cause minimal impairment, when the diagnosis is uncertain, when the family chooses not to use medication for the child, or as an adjunct to medication treatment.

Behavior management in the home is most effective when parents understand the principles of the approach. The clinician may help the parent better understand behavior management, and parent training programs are available in many communities. These programs help parents understand their child's behavior and provide tools to deal with behavioral difficulties. Behavioral therapies have proven effective when consistently implemented and maintained. Additional forms of therapy, such as cognitive-behavioral therapy or family therapy, although not proven to be effective in the management of core ADHD symptoms, may be appropriate in the treatment of comorbid problems or family interaction difficulties.

Table 5. Approved Medications for the Treatment of Attention-Deficit/Hyperactivity Disorder in Children 6 Years of Age and Older

Brand/Generic	Form/Units Available	Starting Dose	MRD	Comment
Methylphenidate (MPH)				
Ritalin®*/MPH (Novartis, East Hanover, NJ)	5-, 10-, 20-mg tab (scored)	5 mg bid to tid	60 mg	Rapid onset (within 15 to 20 min), rapid termination of action. Lasts 3.5 to 4 h**
Ritalin SR®*/MPH (Novartis, East Hanover, NJ)	20-mg tab (sustained release: half released immediately, half released 4 h later)	20 mg q AM	60 mg	Effect usually lasts about 8 h.** Must be swallowed whole; cannot be crushed or chewed.
Ritalin LA®/MPH (Novartis, East Hanover, NJ)	10-, 20-, 30-, 40-mg caps, extended-release (50% immediate release beads; 50% modified release beads; bimodal release profile)	10 mg q am; increase by 10 mg each week until good control is achieved	60 mg	May sprinkle contents on applesauce and swallow without chewing beads (contents should not be crushed, chewed, or divided). Lasts 8 to 10 h.**
Concerta®/MPH (ALZA, Mountain View, CA [marketed by Mc Neil])	18-, 27-, 36-, 54-mg tabs (immediate-release outer coating; osmotic pressure system delivers drug gradually)	18 mg q AM; increase weekly by 18 mg each week until good control is achieved.	72 mg	Noncrushable; must be swallowed whole. Lasts 12 h.** Note: nonabsorbable outer shell may be seen in stool; avoid with gastrointestinal narrowing.
Metadate CD®/MPH (UCB, Rochester, NY)	10-, 20-, 30-, 40-, 50-, 60-mg cap extended-release (30% immediate release, 70% gradually; bimodal peaks at 1½ and 4½ h)	20 mg q AM and increase by 10 mg each week	60 mg	Note: may sprinkle contents on applesauce.
Methylin®/MPH (AlliantPhr, Alpharetta, GA)	2.5-, 5-, 10-mg tab (chewable); 5 mg/5 mL,10 mg/5 mL (oral solution)	5 mg bid with increments of 5 to 10 mg weekly	60 mg	
Focalin®/dexMPH (Novartis, East Hanover, NJ)	2.5-, 5-, 10-mg tabs	2.5 mg bid; increase in 2.5- to 5-mg increments	20 mg	
Focalin XR®/dexMPH (Novartis, East Hanover, NJ)	5-, 10-, 15-, 20-mg caps extended-release (bimodal peaks 4 h apart)	5 mg q AM; increase weekly by 5 mg	20 mg	May sprinkle contents on applesauce and swallow without chewing beads.
Daytrana®/MPH (Shire US, Wayne, PA)	10-, 15-, 20-, 30-mg transdermal patch	Apply 2 h before desired effect; remove after 9 h (may remove earlier)	30 mg	Hypersensitivity to methylphenidate, especially when patch not removed after 9 h. MRD 30 mg/day.

(Continued)

Complementary and Alternative Therapies

Numerous complementary and alternative treatments exist for ADHD, but a comprehensive review is beyond the scope of this article. Common dietary interventions include elimination of foods (such as sugar) or food additives (such as dyes) or addition of dietary supple-

Table 5. Approved Medications for the Treatment of Attention-Deficit/Hyperactivity Disorder in Children 6 Years of Age and Older—continued

Brand/Generic	Form/Units Available	Starting Dose	MRD	Comment
Amphetamines (AMP)				
Dexedrine®*†/dextroAMP (GlaxoSmithKline, Research Triangle Park, NC)	5-mgtab	5 mg q day or bid and increase of 5 mg weekly	40 mg	For 3 to 5 year olds, 2.5 mg daily and weekly increases of 2.5 mg.
Dexedrine Spansules®/ dextroAMP sulfate (GlaxoSmithKline, Research Triangle Park, NC)	5-, 10-, 15-mg spansule sustained-release caps	5 mg q AM and increase by 5 mg weekly	40 mg	May sprinkle contents on applesauce and swallow without chewing beads.
Adderall®*/mixed AMP salts (DSM Pharm, Greenville, NC)	5-, 7.5-, 10-, 12.5-, 15-, 20-, 30-mg all scored	5 mg 1 to 2 times/ day and increase by 2.5 mg weekly	40 mg	
Adderall XR®*/mixed dextroAMP/AMP salts (Shire US, Wayne, PA)	5-, 10-, 15-, 20-, 25-, 30-mg caps extended-release (50% immediate release bead; 50% beads release 4 h later; biphasic model)	10 mg q AM and increase by 10 mg weekly	40 mg	May sprinkle contents on applesauce and swallow without chewing beads.
Desoxyn®/Met AMP HCl (Abbott Pharmaceuticals, Deerfield, IL)	5-mg tab	5 mg 1 to 2 times per day, increase by 5 mg weekly	20 to 25 mg	
Vyvanse® Lisdex AMP dimesylate (Shire US, Wayne, PA)	20-, 30-, 40-, 50-, 60-, 70-mg caps	20 mg q AM	70 mg	May sprinkle contents in a glass of water; needs to be consumed immediately.
Nonstimulant				
Strattera®/Atomoxetine (Eli Lilly, Indianapolis, IN)	10-, 18-, 25-, 40-, 60-, 80-, 100-mg caps (cannot be opened)	<70 kg: Start 0.50 mg/kg q AM×4 days; increase to 1 mg/kg po q AM×4 days, then to 1.2 mg/kg per day in single or bid dose; assess response in 2 wk. >70 kg: Start 40 mg po q AM×4 days; increase to 80 mg po q AM (or 40 mg po bid); assess response in 2 wk.	1.4 mg/kg per day or 100 mg	

MRD: maximum recommended daily dose
*Generic forms available.
**Note: durations of action are estimates; duration may vary with individual child.
†Dexedrine is approved in children 3 to 5 years of age.
Note: drugs listed do not appear in order of importance. *Pediatrics in Review* does not imply endorsement of any product. Recommendation does not serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.
Resource: Accessed October 2009 at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm107918.htm

ments (egs, vitamins, minerals, herbs). Elimination of sugar has not proven to have an observable effect. Although new treatments for ADHD would be a welcome addition to pharmacologic and behavioral intervention, more evidence-based research needs to be conducted before complementary and alternative therapies can be recommended for the daily management of children who have ADHD.

Table 6. Contraindications to Medications Used for Treatment of Attention-Deficit/Hyperactive Disorder

Active Ingredient	Contraindication
Mixed salts of amphetamine	Monoamine oxidase (MAO) inhibitors within 14 days, glaucoma, symptomatic cardiovascular disease, hyperthyroidism, moderate-to-severe hypertension
Dextroamphetamine	MAO inhibitors within 14 days, glaucoma, symptomatic cardiovascular disease, hyperthyroidism, moderate-to-severe hypertension
Methylphenidate	MAO inhibitors within 14 days, glaucoma, symptomatic cardiovascular disease, hyperthyroidism, moderate-to-severe hypertension, pre-existing severe gastrointestinal narrowing; use caution when prescribing concomitantly with anticoagulants, anticonvulsants, phenylbutazone, and tricyclic antidepressants
Atomoxetine	MAO inhibitors within 14 days, glaucoma; may interfere with selective serotonin reuptake inhibitor metabolism (uses CYP2D6 system); drug interaction with albuterol; jaundice or laboratory evidence of liver injury

Adapted from *Caring for Children with ADHD: A Resource Toolkit for Clinicians*. 2002.

Follow-up and Long-term Management

Children who receive ADHD diagnoses require long-term follow-up because evidence is increasing that ADHD does not resolve as children get older. Long-term management includes adhering to the principles of treatment discussed previously.

The clinician, family, and school professionals are responsible for joint assessment and treatment of the comorbid conditions associated with ADHD. For example, if academic performance is an ongoing concern despite treatment for ADHD, the clinician may want to empower the family to request that the school evaluate the child for a possible learning disorder. Screening for comorbid mental health conditions may prompt the primary care clinician to refer the child to clinicians specially trained in assessing and managing such conditions.

In general, stimulants are effective for treating ADHD symptoms in children who present with comorbid anxiety or depressive disorder, although additional treatments (psychotherapy or medication treatment) often are needed. Children who have intellectual disability receive the diagnosis of ADHD if their symptoms are inconsistent with their developmental level and cause additional functional impairments.

The evaluation of a lack of response to treatment should include determining whether the set target goals are realistic and target behaviors clearly defined, re-evaluating the original diagnosis of ADHD, and screening for and treating any comorbid conditions. Lack of

Table 7. Effective Behavioral Techniques for Attention-Deficit/Hyperactivity Disorder

Technique	Description	Example
Positive reinforcement	Providing rewards or privileges contingent on the child's performance	Child completes assignment and is allowed to play on the computer
Time out	Removing access to enjoyable activities because of unwanted or problem behavior	Child hits sibling impulsively and is required to sit for 5 minutes in time out
Response cost	Withdrawing rewards or privileges contingent on performance of unwanted or problem behavior	Child loses free time privileges for not completing homework
Token economy	Combining positive reinforcement and response cost	Child earns stars for completing assignments and loses stars for getting out of seat. The child cashes in the sum of stars at the end of the week for a prize

Adapted from AAP Clinical Practice Guideline. Treatment of the school-aged child with ADHD. *Pediatrics*. 2001;108:1033–1044.

adherence to treatment also may be a factor or a change in medication may be warranted. Medication failure may prompt use of a second-line medication or referral to specialists for consultation and treatment when adequate trials of both groups of stimulants have failed.

Prognosis/Long-term Outcome

As children age, their hyperactive and impulsive symptoms tend to decrease. Despite these changes in symptoms, most children continue to meet criteria for ADHD as adolescents and adults. However, the treatment goals and objectives need to be modified over time. Academic problems may become more obvious and require additional interventions as children grow older. Children whose ADHD is untreated also are at increased risk for developing substance abuse problems and other high-risk behaviors. Comorbid conditions remain present and require ongoing monitoring.

To view References, a Suggested Reading list, and books and resources for families for this article, visit http://pedsinreview.aappublications.org and click on the article title.

Summary

- Based on strong research evidence, school-age children who present with behavior problems or academic underachievement should receive an evaluation for ADHD. (2)(5)
- Based on consensus and strong research evidence, ADHD-specific rating scales may be used to evaluate a child for symptoms of ADHD, but they are not diagnostic of ADHD. (5)(16)
- Based on strong research evidence, approximately 67% of patients diagnosed as having ADHD have comorbid mood disorder or learning disorder. (5)(22)(23)
- Based on strong research evidence, the primary care clinician should establish a treatment program that recognizes ADHD as a chronic condition that requires ongoing management and monitoring. (17)
- Based on strong research evidence, the clinician initially should recommend stimulant medication for the treatment of ADHD, with stimulant drugs from either class (amphetamines, methylphenidate) being equally effective. (17)

PIR Quiz

Quiz also available online at http://pedsinreview.aappublications.org.

5. An association has been found between ADHD and:

   A. Ethnicity.
   B. High birthweight.
   C. Lead exposure.
   D. Race.
   E. Socioeconomic status.

6. According to Section 504 of the Rehabilitation Act of 1973, an educational modification that is *not* allowed is:

   A. Modified homework assignments.
   B. Motor breaks from classroom routine.
   C. Preferential classroom seating.
   D. Reminders to stay on task.
   E. Special education services.

7. Of the following, the statement about medication management for ADHD that is *not* correct is that:

   A. Dosing of medication is not weight-dependent.
   B. Extended-release preparations are preferred for older children.
   C. Medication effects are dose-dependent.
   D. Medication should be initiated after behavioral management fails.
   E. Teacher rating scales are useful during the titration phase.

8. Of the following, the *least* common adverse effect of stimulant medication is:

   A. Abdominal pain.
   B. Headache.
   C. Irritability.
   D. Sleep disturbances.
   E. Weight gain.

9. A true statement about tics that occur after the start of stimulant medication is that:

   A. Improvement in symptoms may outweigh the impairment caused by the tics.
   B. Stimulant medication is a well-established cause of tics.
   C. The drug dose should be decreased as soon as tics appear.
   D. The onset of tics and the use of stimulant medication are unrelated.
   E. The presence of tics is a contraindication to stimulant use.