

CHAPTER 13

Attention-Deficit/Hyperactivity Disorder

Attention-deficit/hyperactivity disorder (ADHD) is the most prevalent neurobehavioral disorder of childhood and one of the most common chronic conditions in school-age children. It is characterized by symptoms of age-inappropriate inattention, motor restlessness, hyperactivity, distractibility, poor impulse control, or a combination of these symptoms. It is typically diagnosed in childhood and impacts behavioral, emotional, cognitive, and social domains. Without optimal treatment, ADHD can have long-term implications, including decreased likelihood of high school and postsecondary graduation as well as poor peer relations.

ETIOLOGY

ADHD is multifactorial in origin with certain prenatal exposures, genetic, neural, and environmental contributions. Many studies suggest strong but variable degrees of genetic associations with ADHD. Twin and family studies demonstrate high heritability and greater risk of developing ADHD in first-degree relatives, especially those where ADHD persists into adolescence and adulthood. Two candidate genes have been primarily implicated regarding the development of ADHD: dopamine transporter gene (*DAT1*) and the dopamine 4 receptor gene (*DRD4*).

Neuroimaging studies have demonstrated structural differences, including smaller cortical volumes, small-volume reduction throughout the brain, and abnormalities of the cerebellum especially with the midline and vermal elements in

patients with ADHD. However, these findings overlap with findings of other conditions; therefore imaging is not useful in the general diagnosis of ADHD. Imaging studies have also identified functional differences in patients with ADHD, including overall delay in cortical maturation and dysregulation of the frontal subcortical circuits, suggesting that the pathophysiologic features include large-scale neuronal networks including frontal to parietal cortical connections.

Environmental links have been described with prenatal exposure to a variety of substances, including nicotine, alcohol, prescription medications, substances of abuse, lead, organophosphate pesticides, and polychlorinated biphenyls. Additionally, central nervous system injury from trauma or infection increases the risk of ADHD.

EPIDEMIOLOGY

Prevalence rates for ADHD vary depending on research methodologies used, the population studied, and changing diagnostic criteria. Worldwide ADHD prevalence in children is 7.2%. In the United States, 9.4% of children aged 2–17 years, including 2.4% of children aged 2–5 years, have had a diagnosis of ADHD. Symptoms consistent with motor restlessness and aggression are more commonly seen in preschool children, while symptoms of disorganization and inattention are more often noted in older children and adolescents. The male:female ratio is greater than 2:1. Girls with ADHD are more likely to be diagnosed with anxiety or depression, while boys tend to have comorbidities such as oppositional defiant disorder. Symptoms of ADHD, particularly impulsivity and inattention, frequently persist past childhood, with up to 80% of those affected having symptoms into adolescence and 40% into adulthood.

Clinical Symptoms

Many of the symptoms of ADHD mimic typical findings of normal development. Thus it is important to consider the child's symptoms in the context of typical, atypical, and abnormal development. The symptoms to meet the *Diagnostic and Statistical Manual of Mental Health Disorders*, Fifth Edition (DSM-5) criteria must be developmentally inappropriate, and the onset of these symptoms should be before the age of 12. Symptoms of inattention (e.g., failing to pay close attention to details, appearing to not listen when spoken to directly, executive functioning skills' concern), hyperactivity (e.g., being fidgety or restless, leaving a seat when expected to remain seated), or impulsivity (e.g., blurting out and interruption) may indicate a diagnosis of ADHD (Table 13.1).

Diagnosis and Evaluation

Universal screening for ADHD is not recommended. The DSM-5 led to an expanded window of the age of onset with broader-based criteria. ADHD is diagnosed in the clinical setting after a full evaluation with a history and a full physical exam. The **history** should rely on open-ended questions to explore specific behaviors and their impact on academic performance, family and peer relationships, safety, self-esteem, and daily activities. Ultimately, a diagnosis of ADHD requires that the symptoms be measured with valid rating scales to establish the diagnosis. These rating scales should

TABLE 13.1 Key Diagnostic Symptoms of Attention-Deficit/Hyperactivity Disorder

INATTENTIVE SYMPTOMS	
•	Does not give close attention to details or makes careless mistakes
•	Has difficulty sustaining attention on tasks or play activities
•	Does not seem to listen when directly spoken to
•	Does not follow through on instructions and does not finish schoolwork, chores, or duties in the workplace
•	Has trouble organizing tasks or activities
•	Avoids, dislikes, or is reluctant to do tasks that need sustained mental effort
•	Loses things needed for tasks or activities
•	Easily distracted
•	Forgetful in daily activities
HYPERACTIVITY OR IMPULSIVITY SYMPTOMS	
•	Fidgets with or taps hands or feet, or squirms in seat
•	Leaves seat in situations when staying seated is expected
•	Runs about or climbs when not appropriate (may present as feelings of restlessness in adolescents or adults)
•	Unable to play or undertake leisure activities quietly
•	“On the go,” acting as if “driven by a motor”
•	Talks excessively
•	Blurts out answers before a question has been finished
•	Has difficulty waiting to take turns
•	Interrupts or intrudes on others

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reflect performance in at least two settings such as in school and in home.

Clinical guidelines emphasize the use of DSM-5 with specific criteria to diagnose ADHD (<http://www.cdc.gov/ncbddd/adhd/diagnosis.html>). Symptoms generally should be present prior to 12 years of age with evidence of significant impairment per rating scales in social, academic, or work settings; additionally, other mental health disorders must be excluded. Changes incorporated into the DSM-5 diagnostic criteria include the age prior to which symptoms must occur (to identify the subset of older children, mainly female, who exhibit predominantly inattentive symptoms, which may not be noted until adolescence), as well as the need for symptoms in at least two settings.

A **physical examination** is essential to identify medical (e.g., neurologic, genetic) or developmental problems (e.g., cognitive impairment, language disorder, learning disability, autism spectrum disorder) that may underlie, coexist, or provide an alternative explanation for the child's behaviors.

Pertinent laboratory tests to evaluate for other disorders should be considered based on the relevant history and clinical components. Consider thyroid function studies, blood lead levels, genetic studies, anemia screening, or other evaluation if indicated by medical history, environmental history, or physical examination.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis can be challenging. The diagnostic process should evaluate for other conditions such as sleep disorders, seizure disorders, substance use, thyroid abnormalities, lead intoxication, sensory processing conditions, and vision or auditory deficits—all of which can cause or exacerbate hyperactivity and distractibility. Migraine headaches, asthma, hematologic disorders, and malignancies can also affect attention and impact school performance. Inattention and hyperactivity may also be features of genetic disorders such as fragile X, 22q11.2 deletion syndrome, and neurofibromatosis type 1. Attention must be paid to any medications that could contribute to symptoms of ADHD. Finally, psychologic stress from bullying, abuse, or disruptive surroundings can also lead to symptoms of hyperactivity, impulsivity, and inattention and mimic ADHD. Children who have symptoms of ADHD in only one setting may be having problems due to cognitive disability, level of emotional maturity, or feelings of inadequate well-being in that setting. Overall, it is prudent to investigate and ensure overall well-being, including sleep and nutritional hygiene, before embarking on an extensive evaluation of ADHD.

Co-morbidities

Co-morbidities are often present in children with ADHD, including anxiety (20–25%), learning disabilities (15–25%), developmental language disorders (30–35%), and mood disorders (15–20%). Other co-morbidities and associated conditions include sleep disorders, decreased motor coordination skills, oppositional defiant disorder, conduct disorders, Tourette syndrome, and fragile X syndrome. Close surveillance for co-morbidities is necessary not only at the time of diagnosis but also in the longitudinal management of ADHD.

Treatment

Management begins with recognizing ADHD as a chronic condition and educating affected children and their parents about the diagnosis, treatment options, and prognosis. A management plan should focus on achievable outcomes (such as improved relationships, increased academic performance, or fewer classroom interruptions) jointly agreed upon by the parent, the school, and the child.

Treatment strategies vary with age. A majority of children have significant response to a multimodal-treatment approach that includes behavior and academic interventions and medications when appropriate. Anticipatory guidance provides proactive strategies to mediate adverse effects on learning, school functioning, social relationships, family life, and self-esteem. Formal parent training interventions and social skills training have been shown to have some impact on ADHD symptomatology. Management of co-morbidities (such as sleep disorders, anemia, mood disorders, and learning disabilities) is needed for the optimal management of ADHD. In addition, guidance should be given on general nutrition and the use of screen time.

Behavioral therapy is central to children of all ages with ADHD and is the core of overall treatment. **Behavioral management** includes establishment of structure, routine, consistency in adult responses to behaviors, and appropriate behavioral goals. Children also benefit when parents and clinicians work with teachers to address the child's needs. Regular

behavior report cards and other “check-in” aids may be helpful to the child in the respective environments within a classroom or for the overall school day. Behavioral management strategies such as organizational skills training for the older child can enhance executive function skills.

The pediatrician should advocate for **optimal educational settings** in the school. Children may qualify for individual education plans where school psychologists can establish organizational plans and charts for the individual child as part of a management plan. Social skills training or additional mental health interventions may assist some children with behavior change or preservation of self-esteem, particularly when they have coexisting developmental or mental health conditions also requiring treatment.

Medications

Medication-based treatments have been studied rigorously and have been shown to be effective in combination with developmental psychosocial interventions. Behavioral management alone is the standard of care for the preschool child age group. However, non-pharmacologic treatments alone, for the older child and young adult, are not as effective as previously thought.

The clinician should balance the benefits and risks of initiating treatment in the preschool child, especially in cases where evidence-based behavioral treatments are not available to the child and caregivers. Stimulants have been shown to provide some benefit to preschool-aged children in short-term studies, but the overall guiding principal must rest on behavioral management. Medications can be considered, especially if there is moderate to severe continued disturbance such as a history of injury to other children or caregivers, a strong family history of ADHD, other underlying or associated neurodevelopmental disorders, or if ADHD symptoms may be interfering with the other therapies that the child is receiving.

Stimulant medications (methylphenidate or amphetamine compounds) are the first-line agents for pharmacologic treatment of ADHD. Stimulants improve parent report of quality of life and are associated with improved academic performance and lower rates of co-morbidities such as mood disorders. Stimulant medications are associated with a significant clinical benefit in many areas including decision-making, handwriting, and schoolwork productivity. Stimulant use is also associated with improved reading and math scores, fewer injuries, and overall reduced morbidity and mortality involving motor vehicle accident. In adolescents, the use of extended-release stimulants has a positive impact on evening driving performance.

Stimulant medications are available in short-acting, intermediate-acting, and long-acting forms. Extended-release and long-acting forms are preferred and are considered as first-line therapy for most children and adolescents with ADHD outside of the preschool age group. Extended-release forms correlate with improved medication adherence. It is essential to determine the optimal dose in order to avoid significant side effects or lack of efficacy, both of which can result in poor adherence.

Nonstimulant medications, including atomoxetine (norepinephrine reuptake inhibitor), guanfacine, or clonidine (α -agonists), may be helpful in children and are considered as a second-line medication intervention. They have lower treatment response rates and effect size compared to that of stimulants but may be useful for patients in whom stimulants

are contraindicated, not well tolerated, are ineffective (or only partially effective), or who have a history of substance abuse. Guanfacine chloral hydrate XR has been shown to have some efficacy as a monotherapy regimen or adjunctively with a stimulant medication especially when treating for both ADHD and co-morbid oppositional symptoms in children and adolescents.

Overall, dosing should be based on the individual rather than on the severity of the presentation or the child's age or size. Close monitoring is needed with surveillance for future dose adjustments. The effects of the initial dose should be followed closely within a few days, and then on a weekly basis during the first month of medication initiation.

Information on medication efficacy, associated adverse effects, and appropriateness for various ages continues to emerge. Current information on specific medications is available through the Centers for Disease Control and Prevention (CDC) and American Academy of Pediatrics (AAP).

Medication side effects, including insomnia, loss of appetite, weight loss, jitteriness, and rebound moodiness, are common and are often dose dependent. Medications may exacerbate existing tic conditions. Other potential side effects include dry mouth, dizziness, drowsiness, constipation, euphoria, dysphoria, irritability, agitation, anxiety, hallucinations, mania, social withdrawal, nightmares, headaches, abdominal pain, and medication rebound. Children who are taking medications must be regularly screened for side effects, including careful monitoring of the child's growth. Providers should titrate medication dosages and timing to minimize side effects and optimize treatment response.

Stimulant drugs may be associated with adverse cardiovascular events such as sudden cardiac death in patients with an underlying disorder exacerbated by sympathomimetic agents. While episodes are rare, screening for cardiac disease by history, family history, and physical exam is critical prior to initiation of stimulant medication and with continued surveillance during the ongoing treatment with stimulants.

Complementary Alternative Medicine

Non-traditional interventions are frequently used by families despite a lack of evidence for their effectiveness in children. Practitioners should explicitly ask about the use of alternative medicines including herbal supplements, chiropractic interventions, and meditation/relaxation techniques.

PEARLS FOR PRACTITIONERS

See Behavioral Disorders: Pearls for Practitioners at the end of this section.