



Editors' Comment

Since formal recognition of Attention-deficit/hyperactivity Disorder (ADHD), research scientists and physicians have focused on the hallmark symptoms - hyperactivity, impulsivity and inattentiveness - of individuals with ADHD. This approach has led to the classification of ADHD as a real medical/psychiatric/neurological condition, has improved the reliability of diagnosis, and has resulted in the development of targeted psychopharmacological and behavioral treatments. ADHD has proved to be a manageable disorder; many children and adolescents have been helped to lead positive and satisfying lives. However, the diagnosis of ADHD is still lacking a critical component; it describes the symptoms, but does not inform us about the causes. Many leading researchers in the field, building on the advances in neuro-imaging and knowledge of the brain, believe their focus should shift from description to identification of underlying causes. Since individuals with ADHD differ in the ways they manifest the disorder, research which examines these differences in symptoms can lead to more differentiated and nuanced understanding of symptoms and effective treatment strategies.

In this issue of the NYU Child Study Center Letter, we discuss ADHD in the light of where we've been, what we know at the present time, where we're going, and what the research of the future holds

AG/HSK

ADHD: WHERE WE'VE BEEN AND WHERE WE'RE GOING

Introduction

Attention-deficit hyperactivity disorder (ADHD) is the most commonly diagnosed neuro-behavioral childhood disorder. Prevalence estimates vary, but the general consensus is that 3 - 7.5% of youth are affected. Yet among some segments of the public and the media, ADHD remains one of the most controversial childhood diagnoses, due to an incomplete understanding of the complexity and biological basis of this disorder.

ADHD is a chronic disorder that interferes with a child's ability to regulate activity (hyperactivity), inhibit behavior (impulsivity), and attend to task (inattention). Functional difficulties may occur across multiple settings, and psychological and/or learning disorders are common. The impact on a child's self-esteem may be serious. ADHD symptoms - in varied expression - may persist into adolescence and adulthood.

How Do We Know ADHD When We See It?

Over the years, ADHD has undergone many definitions and labels, yet behavioral characteristics - inattentiveness, hyperactivity and impulsivity - have always defined the major symptoms. To qualify as ADHD, the behaviors should be developmentally inappropriate and

manifest in multiple settings (eg, school, home, and/or social interaction.) Rating scales, checklists, and neuropsychological batteries may provide evidence for the disorder and accompanying conditions. However, there is no single test to diagnose ADHD. Depending on which symptoms predominate, the Diagnostic and Statistical Manual of Mental Disorders IV¹ recognizes the following ADHD subtypes.

- Predominantly inattentive subtype (20% to 30% of ADHD cases)
- Predominantly hyperactive/impulsive subtype (<15%)
- Combined subtype (50% to 75%)

Below are some guidelines that help characterize aspects of the ADHD subtypes:

- **Inattentive features:** careless mistakes, difficulty sustaining attention, failure to listen, failure to finish tasks, difficulty organizing tasks, avoiding tasks requiring sustained attention, easily distracted and forgetful.
- **Hyperactive features:** fidgeting, difficulty staying seated, excessive movement (restlessness), difficulty engaging in quiet activities, and excessive talking.
- **Impulsive features:** blurts out comments/answers questions too soon, difficulty awaiting turn, interrupts/intrudes upon others, jumps



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into things, failure to reflect before acting, and excessive talking.

Other symptoms characterizing ADHD include low frustration tolerance, frequent shifts of activities, organizational difficulties, and excessive daydreaming. These symptoms are usually pervasive, although in some settings, the child may function normally, with no apparent impairments. Some children may be gifted and creative in specific domains, yet struggle in others. Today, our knowledge of the biological basis of ADHD has broadened our understanding. In addition to the hallmark behaviors of ADHD, a central feature of the disorder is difficulty with what is referred to as the *executive functions* carried out in the brain. These functions include the ability to organize and control behavior, to plan and to follow through on reaching a goal.

How is normal childhood behavior different from that of children with ADHD? It's a matter of degree and of quality. Typically, all children are normally physically active and curious, and therefore ADHD may present a diagnostic challenge. ADHD symptoms represent extremes (beyond the normative range) on the broad spectrum of normal childhood behavior. Further, the ADHD symptoms must be pervasive and severe enough to cause the child significant difficulties in his or her daily life

ADHD Doesn't Always Look The Same

ADHD is different for boys and girls

Current estimates indicate that ADHD is more common among boys than girls, with a 3-10:1 ratio. Recently, however, we have come to understand that girls may be underdiagnosed due to differences in their presentation. Recent studies report that the inattentive subtype is twice as common in girls than boys, and among

boys, the hyperactive/impulsive subtype is more common. Because inattentive symptoms are often overlooked, girls are more likely to slip through the diagnostic net. With appropriate recognition and treatment, however, girls' symptoms are as likely to improve as those of boys².

ADHD looks different at different ages

Preschool children (ages 3-5) The ADHD behaviors in preschool children can be particularly difficult to distinguish from those of their peers. These behaviors include motor restlessness (as if "driven by a motor"), difficulty completing developmental tasks (e.g., toilet training), decreased and/or restless sleep, insatiable curiosity, family difficulties (e.g., obtaining and keeping babysitters), vigorous and often destructive play, excessive need of parental attention, argumentativeness, delays in motor or language development, excessive temper tantrums (more severe and frequent), low levels of compliance (especially in boys).

School-age children (ages 6-12) Children in this age group face increasing demands both academically and socially. The school-age child with ADHD may be easily distracted, with messy, incomplete homework and careless errors. The child may be disruptive in class and interrupt or intrude on others, have difficulty awaiting turns, display aggression, may often be unable to stay seated, and may appear immature relative to his/her peers. Often, as the child grows older, these symptoms adversely affect academic performance and social interactions. Without intervention, these difficulties may lead to poor self-esteem and depression.

Adolescents (ages 13-18) As the child enters adolescence, hyperactivity may decline, but distractibility and an inner restlessness may continue to present impairments. The impulsive symptoms of ADHD in adolescents tend to be associated with rule-breaking, risky

behavior, conflict with authority figures, poor self-esteem, poor peer relationships, and anger and emotional lability.^{3,4}

ADHD doesn't exist alone

Comorbid disorders are common in youth with ADHD, with more than half presenting with associated disorders, including:

- Oppositional (40% to 60%)
- Conduct (30% to 50%)
- Anxiety (25%)
- Mood (15%)
- Learning (10% to 25%)
- Language and communication disorders also frequently occur.

In youth with bipolar disorder, some estimate that the majority also have ADHD. ADHD confers significant risk for higher rates and younger ages at onset of cigarette smoking and substance abuse^{5,6,7}.

How Does ADHD Affect The Lives it Touches?

Children with ADHD experience challenges across important domains in their lives. Without identification and treatment, ADHD may have serious consequences, including school failure, family stress and disruption, relationship problems, substance abuse, delinquency, increased risk for accidents and job failures. Moreover, the burden of ADHD places critical demands upon the entire fabric of the child's life. Understandably, parents and teachers may be more negative and critical, and they may fail to reinforce the child's appropriate behavior and recognize individual talents. Over time, a range of dysfunctional social patterns may evolve, further exacerbating the challenges.

Family Setting

Family stress is common, as ADHD affects the entire family. Parents may be unsure about appropriate parenting behaviors, and marital conflict

and parenting distress may develop. Divorce or separation is more likely among families with a child with ADHD. Additionally, the added stress of parenting a child with ADHD may be linked to parental alcohol consumption. Parents' preoccupation with problems may interfere with their ability to recognize and encourage special talents.

School Setting

ADHD impacts academic performance in a variety of ways. Children with ADHD are often easily distracted by activities around them, may be unable to sit still in a chair, speak out impulsively, or have difficulty concentrating in large classes. Among children with ADHD who do not receive treatment, school failure is more common, and many are placed in special classes or repeat a grade. More than half of children with ADHD require special tutoring, with rates of associated learning disorders (e.g., math, reading) ranging from 10% to 26%.⁸ However, many children with ADHD have special talents and specific areas of above average intellectual ability or creativity that may be missed.

Social Setting

Difficulties in social functioning, often with peer rejection, are common. Some children with ADHD may be aggressive, impulsive and noncompliant with rules, which may be off-putting to peers. Taking turns and participating in games may be a significant challenge. Typically, however, children with ADHD encounter social difficulty due to an impaired ability to *perform* appropriate social behaviors, rather than a *lack of knowledge* about social skills.

As The ADHD Child Grows Older

Data on adult ADHD are limited (primarily representing males), and due to historical limitations in diagnostic criteria for adults, current studies

may present an incomplete picture of overall adult functioning. One study⁹ that begins to fill this research void followed children with ADHD into young adulthood and adulthood in regard to the prevalence of clinical diagnoses. Results indicated that childhood ADHD persists into adulthood, and that those with ADHD, as a group, showed academic, cognitive and social functioning and problematic ADHD symptoms compared to non-ADHD controls. The authors note, however, that these deficits were relative and do not tell the whole story. Of the individuals participating in this study, nearly all were gainfully employed as adults, many as proprietors of successful businesses (auto repair shops, burglar alarm businesses, cookie franchises, bicycle stores, etc.). Furthermore, substantially fewer experienced emotional and behavioral problems as adults. A full two-thirds of the children followed showed no evidence of any mental disorder in adulthood. The authors also noted that childhood ADHD did not regularly preclude the chances of obtaining a higher level education or profession; some attended law school and medical school, while others became accountants and stockbrokers.

What Causes ADHD?

Over 50 years of scientific and clinical research has provided ample data that support our understanding of ADHD as a neurobiological disorder with strong genetic links. Advances in neuro-imaging and genetic studies have provided insight into the way the brain carries out its mission and how brain structures and functioning influence the development of disorders such as ADHD.

Specific chemicals and systems in certain parts of the brain seem to play a role in ADHD. Abnormalities in the brain's

frontal network are thought to account for ADHD symptoms, but the precise neural and pathophysiologic underpinnings are not fully understood¹⁰. The neurotransmitters dopamine and norepinephrine appear to play a role and likely influence the underlying neurochemistry of ADHD. Recent data also suggest a role for the cholinergic system in mediating ADHD, particularly the attention systems¹¹.

For people with ADHD, the brain may be under-aroused in regions involved with planning, foresight, considering alternative responses and behavioral inhibition (executive functions). Medication likely affects these brain areas, increasing neural activity to normal levels.

Additionally, subtle anatomical differences in brain structure and size have been observed between children with ADHD and non-ADHD children. The brains of children with ADHD who have never taken stimulant medication are slightly smaller (total brain volume about 3% less) than those of non-ADHD children. The children who have never taken stimulant medication also exhibited smaller white-matter volume in the brain than those of non-ADHD children. (White matter, which grows thicker as a child matures, consists of fibers that establish long-distance neural connections.) These findings underscore the importance of further research into the relationship between stimulant medication, brain maturation, and amelioration of ADHD symptoms¹².

Today, we have strong evidence of the hereditary transmission of ADHD. Ongoing data from family, genetic, twin, and adoption studies reveal that ADHD runs in families. ADHD is more common among first-degree biologic

relatives; there is a 92% concordance rate among identical twins. Again, the mechanism seems to be rooted in the functioning of chemicals and processes in the brain^{13,14,15}. Ongoing genetic studies are focusing on dopamine D₂ and D₄ receptor subtypes and the dopamine transporter as candidate genes.

In addition to genetic variations or mutations, causative factors include environmental factors and interactions between genes and environment. Environmental factors can include traumatic brain injury and juvenile stroke, as well as severe early neglect and maternal smoking during pregnancy.

Given the accumulating data from different sources, it is now thought that ADHD likely results from the interplay of several factors, with no single factor being necessary or wholly sufficient for causing the disorder.

The field of ADHD research is headed in new directions. For example, with the advances in imaging and understanding of the brain, researchers are exploring new pathways aimed at understanding the *causes* of ADHD, not only its *behavioral manifestations*. This approach is based on the belief that persons with ADHD seem very different, and that different subtypes may be behavioral manifestations of distinct and possibly overlapping causes. For example, some may fidget and interrupt their classmates while others are quiet and daydream a great deal. Or some may seem disorganized and forgetful, and others can't seem to wait for things to happen. These behavioral differences may be indicative of different causes and may lead to different types of treatment. Studies are planned to attempt to define underlying neuropsychiatric

abnormalities by developing endophenotypes, the inherited traits that predict the risk of acquiring a given disease in the way that high cholesterol predicts an increased risk of heart disease¹⁶.

The identification of endophenotypes may predict the risk of ADHD by focusing on measurable characteristics or symptoms and the areas in the brain that are responsible for these functions, such as 1) inhibition, or the inability to stop oneself, 2) delay aversion, or the tendency to choose immediate gratification over delayed gratification, even if the reward for delay is greater, 3) difficulty in estimating time events, and 4) working memory, which allows one to hold a piece of information "online" for a few seconds while other mental processes occur, a function which controls attention and guides decision making and moment-to-moment behavior.

As one example of the kinds of comparisons to be made, the researchers point out that individuals with different types of ADHD, or manifestations of symptoms, differ in response to stimulant medication. They note that making distinctions at a fundamental level will lead to the development of more effective treatments and sound prevention efforts.

Management and Treatment

Management of ADHD includes both non-medical and pharmacologic intervention, but, for most, medication has been shown to be the strongest predictor of success. While behavioral therapies are reportedly sometimes helpful, their benefits are not as effective as medication. Studies report that the combination of medication

with behavioral therapy is not superior to medication alone, and behavioral therapies alone are inferior to medication¹⁷. However, for certain types of secondary effects such as poor peer relationships and disruptions in the family, parent, child and family intervention may enhance success. In addition, a therapeutic alliance among parents, child and school to ensure interventions are implemented consistently is important.

Non-Medical Interventions

Although medical management is a crucial aspect of treatment, the individual needs of each child may vary, and a case-by-case approach may yield the best results. As an adjunct to medication, the following interventions may be useful:

- **Family-focused interventions:** parent training, couples counseling, and family therapy
- **School-focused interventions:** increased structure, classroom and teaching modality modifications, predictable routine, learning aids, resource room time, and regular homework checks
- **Child-focused interventions:** social skills training, social entry, conversational skills building, conflict-resolution and problem-solving training, anger-control training, and summer treatment programs

Parents can play a critical role in the success of the child with ADHD; they should have frequent communication with the child's teacher, guidance counselor and/or school psychologist. Specialized educational planning, with frequent re-evaluation of the child's progress in school are important. Similar modifications in the home environment can help optimize the child's ability to do homework.

Many children have accompanying

learning disorders, necessitating an individualized remediation plan. Schools are federally mandated to perform an appropriate evaluation if a child is suspected of having a disability that impairs academic functioning. The Individuals with Disabilities Act (IDEA) guarantees appropriate services and public education to children with disability (age 3 to 21); ADHD is a qualifying condition. Behavioral therapy may be helpful when the child has coexisting disruptive behavior, inflexibility, anxiety, or outbursts. Social skills remediation for improving interpersonal interactions and educational coaching for improving organizational and study skills may yield positive results.

Medication Management

For most children with ADHD, medication management is a central part of an effective treatment plan¹⁸. Psycho-stimulants have broad positive impact on classroom behavior, academic performance, interactions with peers and adults, and non-compliant and aggressive behavior. Overall, with dosage adjustments, 75% to 90% of children respond favorably to medication. Clearly, not all children tolerate medications, respond sufficiently, or maintain their response over time; therefore an individualized treatment plan should be adapted accordingly. Medications used for the treatment of ADHD are:

Stimulants. Based on efficacy and safety in >250 controlled trials, stimulants are considered first-line agents. Stimulants increase intrasynaptic concentrations of catecholamines (primarily dopamine). The most commonly used drugs in this class include methylphenidate (Ritalin, Concerta, Metadate) and amphetamine (Adderall, Dexedrine). These medications are available in both immediate- and extended-release formulations. Extended-release, once-daily formulations eliminate

the need for in-school dosing, avoid social stigma, and reduce rebound effects. Children who do not respond well to one stimulant therapy may respond favorably to another.

Adverse effects are usually predictable and manageable: appetite suppression, insomnia, edginess, and gastrointestinal upset. While early reports raised concerns over a stimulant-associated decrease in growth in the height of children, subsequent studies have not confirmed this finding. A recent study suggests that growth deficits may represent maturational delays related to ADHD itself rather than to stimulant treatment.

A common concern among parents is that stimulant treatment will increase the risk for substance abuse disorders, but there is no evidence to support this association. In fact, studies report that stimulant treatment of ADHD reduces the risk for substance abuse over the lifespan by half. Furthermore, there is minimal evidence indicating that stimulant-treated children with ADHD abuse their medication.

Noradrenergic agents (nonstimulant).

A relatively new therapeutic strategy for the management of ADHD, atomoxetine (Strattera) is a highly specific presynaptic noradrenergic reuptake inhibitor. This medication choice may be useful for children who do not tolerate or respond to stimulants. Efficacy has been demonstrated in all subtypes of ADHD. While the therapeutic benefit of stimulants is usually immediate, the effects of atomoxetine may require several weeks.

Antidepressants. Generally considered second-line drug choices for ADHD, the tricyclic antidepressants (imipramine, desipramine, nortriptyline) block the reuptake of neurotransmitters, including norepinephrine. Tricyclics may be effective in controlling abnormal behaviors and improving cognitive

impairment associated with ADHD, but less so than stimulants.

Bupropion (Wellbutrin), a unique agent with indirect dopamine and noradrenergic effects, has been shown to be effective for children with ADHD; bupropion is often used as an initial agent for complex ADHD patients with substance abuse or mood disorders.

Selective serotonin-reuptake inhibitors (Prozac, Zoloft) have not demonstrated efficacy for ADHD, but they may be useful for accompanying mood or anxiety disorders. Venlafaxine (Effexor) may be useful in some cases due to its effect on noradrenergic reuptake inhibition.

Antihypertensives. Clonidine and guanfacine, specifically, are sometimes used to treat the hyperactive/impulsive symptoms of ADHD. They may be particularly useful for associated tics, oppositional behavior, and sleep disturbances.

Meanwhile, new and combination regimens are under continual development for the treatment of ADHD. New isomers (eg, Focalin, the isomer of methylphenidate) and delivery systems (skin patches) offer promise for patients who cannot tolerate current therapies.

A Promising Future

The news is good for children with ADHD. Despite controversies, science has yielded a solid body of knowledge delineating the neurobiological basis of ADHD. Hundreds of clinical trials have demonstrated that medication management is the most important variable for achieving a positive outcome. For certain types of secondary effects, such as poor peer relationships and family stress, parent, child and family interventions may enhance success. Today, more than ever,

we are uniquely positioned to recognize the challenges these children face and to value the gifts they often possess.

Early intervention offers children with ADHD the best opportunity to develop to optimal potential. It is hoped that current research directions which focus on identifying the causes of ADHD will lead to the development of more effective treatments and prevention strategies

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www.aap.org/policy/ac0002.html

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