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ADHD

From childhood to young adulthood

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Abstract: Attention-deficit hyperactivity disorder (ADHD) affects approximately 11% of children between the ages of 4 and 17 years. This article discusses performing a comprehensive assessment for ADHD, the use of validated tools to make an accurate diagnosis, physical exam findings that may be suggestive of certain conditions, and ADHD treatment options.

Attention-deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders NPs will encounter. ADHD affects 6.4 million (11%) school-aged children 4 to 17 years old in the United States.[1] The rate of ADHD diagnosis increased by 42% between 2003 and 2011.[2] The average age at diagnosis is 7 years, and nearly 75% of patients are diagnosed before age 9 years.[1] If a diagnosis is made earlier in life, the ADHD symptoms are more severe.[1]

Males tend to be diagnosed with ADHD at twice the rate of females, but females are most often diagnosed with a predominantly inattentive presentation.[3] Females with

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ADHD have higher rates of comorbid conditions, including internalizing conditions (such as anxiety and depression) and externalizing conditions (such as oppositional defiant disorder and conduct disorder) when compared with females without ADHD.[4]

Black and Hispanic children are diagnosed and treated for ADHD at a significantly lower rate than White children, and these rates often persist through the 10th grade. This pattern could be due to underreporting symptoms in Black and Hispanic communities, which warrants more universal screening for ADHD symptoms. This difference is not thought to be due to overdiagnosis of White children.[5]

There are well-established lifespan trends for ADHD. In childhood, ADHD symptoms are more commonly identified with hyperactive and impulsive symptoms. As individuals age into adolescence and young adulthood, the symptoms of hyperactivity and impulsivity become less pronounced, but the symptoms of inattention persist and continue to cause impairment.[6] Individuals who are diagnosed with ADHD still meet criteria in 60% to 85% of adolescents and approximately 50% of adults.[7]

ADHD rates worldwide affect 8% to 12% of the population.[8] These worldwide data are supported by the strong hereditability of ADHD among all individuals. Twin studies from across the globe confirm that ADHD is inherited in nearly 80% of the offspring of parents with ADHD.[9] ADHD also has one of the strongest genetic associations among all psychiatric conditions across the globe.[9]

Neurobiology and neurochemistry of ADHD

ADHD is a complex disorder that affects nearly all regions of the brain. The prefrontal cortex (PFC) is usually implicated in ADHD and is where executive functioning is housed. Executive functioning is the ability to plan and solve problems; it has been described as working memory, temporal information processing, and response inhibition. It predominates the hyperactive and impulsive symptoms of ADHD.[10]

The PFC malfunctions in children with ADHD, which accounts for hyperactive symptoms.[6] Impulsive symptoms of ADHD appear to be related to the orbitofrontal cortex.[6] Studies have also implicated the cerebellum and basal ganglia as being involved with symptoms of hyperactivity and impulsivity associated with ADHD.[11]

Inattention symptoms of ADHD have been described as problems with selective attention, sustained attention, and response precision. Cognitive flexibility impairment can account for both inattentive and hyperactive symptoms in ADHD.[10,11] Impaired selective attention and sustained attention seen in ADHD have been found in the dorsal anterior midcingulate cortex and dorsal anterior cingulate cortex, using functional magnetic resonance imaging (fMRI) and neuropsychological testing.[12] fMRI has also identified impairment with sustaining attention and smoothly shifting from one topic to the next (cognitive flexibility) within the dorsolateral PFC.

Dopamine has long been implicated in ADHD and continues to be a target of medication therapy for ADHD.[13] Dopamine is primarily synthesized in the midbrain (in the substantia nigra) and is transported to various parts of the brain to include the PFC, caudate, putamen, nucleus accumbens, amygdala, hippocampus, and cerebral cortex. Dopamine D1 and D2 receptors are important for working memory and cognitive flexibility, respectively.[9]

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Gamma-Aminobutyric acid is a significant neurotransmitter in ADHD and is responsible for nearly 70% of all inhibition of the dopamine signal, which results in downstream effects of the entire dopamine system.[10] Norepinephrine in the locus coeruleus also plays a significant role in sustained attention symptoms in ADHD.[9] Cognitive flexibility symptoms in ADHD are linked to acetylcholine in the PFC along with D2 receptors. Serotonin in the basal ganglia and PFC appear to influence how an individual can delay rewards, which is grossly impaired in ADHD.[10,11] Skilled NPs will use this information when assessing and treating ADHD in children, adolescents, and young adults.

Assessment of ADHD

ADHD is a clinical diagnosis characterized by three symptom clusters of inattention, hyperactivity, and impulsivity. Individuals who have ADHD are identified as

having a predominate presentation in either inattention, hyperactivity and impulsivity, or both.[3,14] Primary care providers and pediatricians diagnose approximately 50% of children with ADHD, psychiatrists and psychologists make the diagnosis for the other 50%.[14]

Given the recognized shortage of psychiatrists in the United States, the integration of mental health into primary care is beneficial for children throughout young adulthood, so the ability to assess, diagnosis, and treat ADHD in primary care practices is essential for NPs.[15]

Individuals of all ages should undergo a comprehensive assessment to determine an accurate diagnosis of ADHD and assess for the presence of possible risk factors for ADHD or the presence of comorbid conditions.[16,17] The use of behavioral screening tools provides objectivity to the assessment and should be used as part of the evaluation.[16]

NPs should initiate an evaluation for ADHD for children who present with academic or behavioral conditions that interfere with functioning and have symptoms of inattention, hyperactivity, or impulsivity during the ages of 4 to 18 years.[16] The diagnosis of ADHD should follow established guidelines in *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition (DSM-5), including the requirements for symptom documentation over time, in more than one major setting, and by one or more parent, guardian, teacher, or another adult who works closely with the child.[3,16] Adolescents with ADHD symptoms may be assessed during adolescence and considered positive if symptoms are present between the ages of 7 to 12 years.[16]

The assessment should be comprehensive and identify the chief complaint, symptoms of ADHD, academic problems, behavioral conditions, and the level of functional impairment.[18] An extensive medical history should be obtained to identify the presence of risk factors or comorbid conditions (see *Comorbid conditions and risk factors associated with ADHD*).[19] A review of systems with a focus on diet, sleep, activity level, and elimination may reveal dietary patterns that may not support optimal health or elimination problems, such as enuresis or encopresis. Delayed sleep onset or variable sleep routines may affect overall health.

Because ADHD has a strong genetic propensity, it is important to obtain a complete family medical and psychiatric history.[16,17] Exposure to toxic stressors such as child maltreatment, violence, and family and community stressors should be identified to incorporate knowledge of them into any treatment plan. Parental or child adverse events should also be assessed.[19] Parenting practices and how parents address the child's behavioral concerns should be identified.[20]

A comprehensive social history, including an understanding of the child's environment and how ADHD is affecting family members, should be obtained. How the child is functioning in the home, school, and community will provide the NP with insight into the severity of ADHD symptoms.[16]

A complete physical exam, including a neurologic exam, should be obtained for all children being evaluated for an ADHD diagnosis.[16,18] The NP should examine the child for any dysmorphic features to rule

Comorbid conditions and risk factors associated with ADHD[3,4,19]

Comorbid conditions

- Learning disorders
- Communication disorders
- Intellectual disabilities
- Behavioral conditions including oppositional defiant and conduct disorders
- Motor disorders such as Tourette syndrome and other tic disorders
- Autism spectrum disorder
- Internalizing disorders (anxiety and depression—often greater in females)
- Mood disorders including unipolar depression and bipolar disorder
- Posttraumatic stress disorder
- Substance-related and addictive disorders

Risk factors

- Family medical history of ADHD or another mental health disorder
- Prenatal and perinatal factors, including premature birth and low birth weight
- Genetic disorders such as fragile X syndrome, tuberous sclerosis
- Sleep disorders including obstructive sleep apnea and inadequate sleep
- Seizure disorders or other neurologic disorders

Socioeconomic and environmental risk factors

- Parenting practices
- Teacher-child interactions
- Exposure to adverse childhood experiences
- Child maltreatment
- Poverty, food insecurity
- Parental pathology
- Exposure to severe, early social deprivation
- Maternal drug use, alcohol use, or smoking during pregnancy
- Exposure to environmental toxins such as lead

out a genetic disorder.[18] Growth parameters and body proportion should be evaluated. There is no evidence for using lab tests or imaging studies in diagnosing children with ADHD.

The next step in the assessment is to obtain symptom documentation over time and in more than one major setting (for example, home and preschool/school). The National Institute for Children's Health Quality (NICHQ) developed the Vanderbilt Assessment Scales for initial evaluation and follow-up of ADHD in preschool and school-age children (between ages 6 to 12 years). The scales are available at no cost through the NICHQ (www.nichq.org/sites/default/files/resource-file/NICHQ_Vanderbilt_Assessment_Scales_0.pdf).[21]

The scales also screen for coexisting conditions (conduct disorder, oppositional-defiant disorder, anxiety, depression) and allow the NP to validate and differentiate ADHD presentations. These presentations are based on the *DSM-5* criteria and predominant symptom patterns for the past 6 months, including combined presentation, predominantly inattentive presentation, and predominantly hyperactive/impulsive presentation. The Conner's Rating Scale-Revised may be used for ADHD assessment and is preferred in some practices; it is validated for children ages 6 to 17 years for teacher and parent forms and 8 to 17 years for self-report forms.[22] A list of other rating scales and checklists to use in the evaluation of children through adulthood are available from the American Academy of Pediatrics (AAP).[22]

In addition to obtaining behavior rating scales, the NP should ask to see report cards and samples of the child's schoolwork; any formal testing performed by school personnel; a description of the child's behavior in the classroom; the child's learning patterns; how the symptoms affect the child's progress at school; ways the teacher has adapted the classroom program to help the child; and whether other conditions contribute to or affect the symptoms.[23] Once a comprehensive history and physical exam have been performed, the NP should formulate a diagnosis.

When interviewing adolescents or young adults who present for a possible diagnosis of ADHD, the NP should perform a comprehensive history and may use the Home Education/Employment, Eating, Activities, Drugs and Alcohol, Sexuality, Suicide and Depression, Safety (HEEADSSS) interview.[24] Obtaining a history regarding alcohol use or a possible substance use disorder should be a priority, and the possibility that the individual may be interested in obtaining stimulants for diversion should be considered.

Clinical practice suggests pornography viewing or excessive gaming may be occurring and should also be included as part of the assessment. Adolescents or young adults who have ADHD continue to have impairment in executive functioning or regulation in self-directed actions to choose, enact, and sustain actions across time toward a goal.[25] This manifests as worse driving records compared with peers of a similar age, with 400% higher rates of speeding citations and crashes than individuals without ADHD.[26] Those taking lisdexamfetamine dimesylate stopped on average 9.1% faster than those taking placebo, which is meaningful because they were measured driving 45 to 65 mph.[26] Adolescents with ADHD who drive while taking medication to treat the disorder have significantly lower rates of accidents and better driving performance compared with those who are not taking ADHD medications. It is estimated that over 22% of motor vehicle accidents of individuals with ADHD could have been avoided if they were taking ADHD medications.[26,27]

Treatment of ADHD involves psychosocial or behavioral management, modifications to the school program, and medication.

Treating ADHD

Treatment of ADHD involves psychosocial or behavioral management, modifications to the school program, and medication.[28] NPs should educate families that ADHD is classified as a neurodevelopmental disorder with underlying biologic and neurologic mechanisms requiring chronic care, and the NP should reassure families that the concepts related to a patient-centered medical home model will be implemented in caring for the child.[16] Parents should be informed that the child's ADHD behavior is not intentional, and behavioral change will need to occur with the family to make accommodations and support the child. Recommendations for treatment will vary depending on the child's age.

For preschool-aged children (ages 4 to 5 years), parent- or teacher-administered behavioral intervention

should be the first line of treatment; medication (methylphenidate) may be considered if first-line treatments are not available or insufficient.[16] For children ages 6 to 11 years, the combination of medication and behavioral interventions have the best outcome.[16] For adolescents (ages 12 to 18 years), an FDA-approved medication should be prescribed, preferably along with behavior therapy.[16]

Many individuals with ADHD have negative interactions with family members, friends, and teachers, and both sides often feel distressed or worried about the behavior. Behavior therapy including behavioral parent training, social skills training, behavioral peer interventions, classroom behavioral management, or parent/family education can help mitigate the effects ADHD has on the child.[28,29] Parent training recognizes that ADHD affects an entire family, and behavioral therapy involving all members of the household may restore balance in effective child behavior management.

Evidence-based parenting programs include New Forest Parenting Programme, Positive Parenting Program, The Incredible Years series, and Parent Child Interaction Therapy.[28,29] Information can be provided either by hardcopy or electronically to parents in regard to evidence-based information on ADHD symptoms and treatment options (see *ADHD provider resources*).

If academic or behavioral issues are present in the child's school, parents may request an evaluation from the school's multidisciplinary evaluation team.[30] Parents must sign permission forms before the evaluation process starts. A comprehensive evaluation should be done within 60 days but may vary from state to state.[30] If the child qualifies for special education services, an individual education plan can be developed. If the child does not meet criteria for special education, a Section 504 Service Plan may be developed, which designates reasonable accommodations in the educational program and related aids and services if deemed necessary (for example, occupational or physical therapy).

Examples of common accommodations include seating at the front of the classroom, supplement verbal instructions with visual or written instructions, trackers/reminders for homework, a schedule, organized teacher assistance, modified test delivery, extended test time, assistance with long-term projects, tailored homework assignments, and/or systematic rewards and consequences.[30]

ADHD provider resources

AAP Healthy Children
www.healthychildren.org
Wide range of information on variety of physical and emotional topics related to ADHD. No cost to access website.

ADDitude Magazine
www.additudemag.com
Wide range of information for both providers and parents. Quarterly magazine available online and in print. Restricts access with charge both for magazine and membership

American Academy of Child and Adolescent Psychiatry ADHD Resource Center
www.aacap.org/aacap/Families_and_Youth/Resource_Centers/ADHD_Resource_Center/Home.aspx
Wide range of information on ADHD and other comorbid psychiatric conditions along with treatment options. Free information for both parents and providers.

Child Mind Institute
https://childmind.org
Provides information on symptoms and treatment of mental health disorders. Excellent parenting suggestions and guides. Section for educators. Includes a symptom checker for parents.

Children and Adults with Attention-Deficit/Hyperactivity Disorder
www.chadd.org
A resource for both parents and providers that includes Home of the National Resource Center for ADHD, ADHD toolkit, information on training opportunities, medications, and natural treatment options and publishes a magazine (*Attention*). Must pay to be a member for full access to their website.

National Alliance on Mental Illness
www.nami.org
Provides information on disorders and treatment. Superior information for family members and caregivers. Has LGBTQ section.

National Institute of Mental Health
www.nimh.nih.gov
Extensive information on symptoms and treatment options. All evidence-based information. Technical information and probably more useful to providers than parents.

Medication options

The use of medication has been shown to be effective in more than 70% of individuals with ADHD.[31] When initiating psychopharmacologic therapy for ADHD stimulant medication should be used as first-line treatment.[16,17] The Multimodal Treatment of ADHD trials showed improvement in symptoms of inattention, hyperactivity, impulsivity, and improvement in disruptive behaviors, with some improvements in

ADHD medications and adverse reactions[42]

Stimulant adverse reactions

Amphetamine-based and methylphenidate-based
- Gastrointestinal (GI) (nausea, emesis, loose stools)
- Headaches (usually transient)
- Appetite suppression (severity can range widely)
- Increased BP and heart rate (HR) (benign if asymptomatic)
- Insomnia (usually seen in long-acting preparations)
- Irritability or other mood changes
- Tics (not due to stimulant treatment)
- Altered growth rate
- Priapism

Nonstimulant adverse reactions

Centrally acting alpha$_2$-adrenergic agonist (extended-release guanfacine and extended-release clonidine)
- GI (nausea, decreased appetite)
- Headaches
- Decreased BP and HR (benign if asymptomatic)
- Sedation and somnolence
- Fatigue

Selective norepinephrine reuptake inhibitor (atomoxetine)
- GI (nausea, vomiting, decreased appetite)
- Headache
- Suicidal ideation
- Hepatotoxicity
- Altered growth rate
- Increased BP and HR
- Priapism
- Fatigue

academic functioning and peer relations with stimulant medications.[32-35]

Methylphenidate-based stimulants work by blocking the dopamine-active transport (DAT) and norepinephrine-active transport (NET), thereby increasing dopamine and norepinephrine in the synapses.[6] Amphetamine-based stimulants work similarly at lower doses than methylphenidate. At higher doses, amphetamine-based medications reverse the flow to the DAT and NET. Because of this, amphetamine-based stimulants are considered twice as potent as methylphenidate-based stimulants.[6]

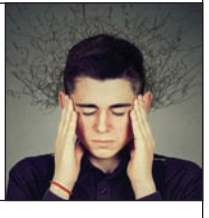
Before prescribing stimulants, recommendations for screening include obtaining a targeted cardiac history, which includes patient history of previously detected cardiac disease, palpitations, syncope, or seizures; a family history of sudden death in children or young adults; hypertrophic cardiomyopathy; and long QT syndrome. In addition, a careful cardiac exam and referral for an ECG or a cardiologist for patients with suspected heart disease or identified risk factors for sudden death should be considered.[36]

There are several formulations of methylphenidate and amphetamine-based medications. All stimulants are thought to be equally effective, but starting with methylphenidate is often recommended with evidence that amphetamines may have a greater risk of adverse reactions.[37] The FDA-approved minimum age for most stimulants is 6 years, but immediate-release dextroamphetamine and mixed amphetamine salts have both been approved starting at age 3 years.[16] Some general principles in prescribing include starting with a low dose and titrating upward ("start low, go slow") to ensure that the child receives the maximum benefit with the fewest adverse reactions.[16] Titration should occur at weekly or every other week.

Atomoxetine, extended-release guanfacine, and extended-release clonidine can be used as second- and third-line medications and are useful alternatives to stimulants in children with comorbid conditions or substance use disorders.[38] Bupropion, an atypical antidepressant that increases the transmission of dopamine and norepinephrine by blocking the reuptake of both neurochemicals, is as effective as methylphenidate in treating ADHD symptoms from age 6 years and up.[6,39,40] In practice, bupropion is FDA off-label for ADHD, it does not have dosage recommendations for pediatric patients with ADHD, and the best effects are seen in patients with ADHD and depressive symptoms as well as those who may have misused a controlled substance.[39,40]

Bupropion is generally well tolerated, but there is a black box warning related to suicidal thoughts and

When initiating psychopharmacologic therapy for ADHD stimulant medication should be used as first-line treatment.



behaviors for use in pediatric patients.[40] Adverse reactions of bupropion include nausea, dry mouth, anorexia, headache, insomnia, tremor, anxiety, weight loss, and increased BP.[41] Modafinil is a dopamine agonist that has evidence of treating ADHD from age 6 years and older.[40] Like bupropion, modafinil is considered a nonstimulant option and is FDA off-label for ADHD that is usually prescribed as a fourth-line treatment option for ADHD. Modafinil is generally well tolerated, and the effects can be seen quickly. Dosing is not well established in pediatric populations.[40] Adverse reactions of modafinil include dyspepsia, nausea, diarrhea, headache, anxiety, and insomnia.

There is a potential for linear growth impairment with psychostimulant medications, so children should be monitored carefully for height and weight.[43] Challenges with medication management include the extended-release medication not lasting long, as some patients are fast CYP450 metabolizers, so these cases may need an immediate-release stimulant prescribed as an afternoon dose (see *ADHD medications and adverse reactions*).

If none of the agents routinely used to treat ADHD are effective, the NP should undertake a careful review of the diagnosis and consider behavior therapy for ADHD treatment and referral of the patient to a psychiatrist or psychiatric mental health NP.[16] Parents require frequent consultation for concerns when starting medication, so practices need to arrange for availability for questions and communication as well as frequent follow-up.

Summary

The role of the NP is to monitor children, adolescents, and young adults with ADHD who are treated with medication regularly, monitoring their height, weight, BP, and pulse, and identify adverse reactions. Periodic assessments should determine if there is a continued need for treatment or if symptoms have remitted, and treatment should continue if symptoms remain present and cause impairment.[16] The NP should monitor school performance, child and family functioning, and make appropriate referrals for diagnosis and treatment. Early and effective identification and treatment of ADHD prevents long-term consequences and can lead to healthy and productive lifestyles for affected patients. NP

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INSTRUCTIONS
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