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Diagnosis and Treatment of Attention Deficit Hyperactivity Disorder

A 5-year-old about to be kicked out of preschool. A quiet 15-year-old struggling to keep organized in high school. A first-year medical student with failing grades. At first glance, there appears to be little in common among this group. However, a closer look reveals that the primary symptoms of dysfunction in each case may stem directly from unrecognized or untreated attention deficit hyperactivity disorder (ADHD).

Presenting with persistent inattentiveness and/or hyperactivity and impulsivity severe enough to interfere with functioning, and occurring in more than one setting, ADHD is one of the most common neurodevelopmental disorders of childhood, with evidence of impairment often continuing into adult years.¹

ADHD also is a disorder surrounded by controversy. Until 2019, the International Classification of Disorders (ICD) did not include the term ADHD and referred instead to “hyperkinetic disorder.” ICD-11 helped clarify global views of ADHD by aligning ICD criteria and nomenclature with the pre-existing *Diagnostic and Statistical Manual of Mental Disorders 5th edition* (DSM-5) ADHD criteria. However, incidence, prevalence, and treatment methods remain variable and appear to be influenced significantly by societal factors, leading some to question the validity of the disorder.²

Lending fuel to the fire, articles, newscasts, and books geared to a lay audience suggest that ADHD is a modern-day condition created by the demands of society, leaving many parents convinced that changes in environment or parenting techniques will “fix” the child.^{3,4} Although there may be some validity to this position, historical papers tell us that ADHD is far from a modern phenomenon; descriptions of children with core symptoms of what we now call ADHD exist as far back as the time of ancient Greece.⁵

Treatment of ADHD remains another area of concern for providers, patients, and families. Stimulant medication is the gold standard of intervention but comes with risks — including the potential for diversion to recreational use and general misuse of this controlled substance. Measurement of response via teacher or parent scales seems uncomfortably subjective to many providers, making it difficult to feel secure in recommending dose changes or adjustments.

Yet, we know that untreated ADHD can have significant negative consequences ranging from poor self-esteem when children are unable to match peers in behavioral expectations, to academic or occupational underachievement and demoralization to relationship problems.⁶

This article reviews best-practice methods for diagnosis and treatment of ADHD from childhood into adult years. A historical view of ADHD is presented, with


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EXECUTIVE SUMMARY

Attention deficit hyperactivity disorder (ADHD) is a disorder surrounded by controversy. Although often considered to be a modern phenomenon, descriptions of children with core symptoms exist as far back as the time of ancient Greece.

- A recent report estimated the worldwide prevalence among children younger than the age of 18 years at 7.2%. A national survey of parents revealed 6.1 million U.S. children ages 2 to 17 years have been diagnosed with ADHD at some point.
- Boys are twice as likely as girls to be diagnosed with ADHD. The median age of diagnosis is 6 years of age for both genders. The persistence rate extending into adulthood varies widely from 14% to 78%.
- Diagnostic tools specific for adults are available. The Adult ADHD Self-Report Scale Symptom List is used frequently. It is available without charge and can be completed in a clinic setting within five to 10 minutes.
- The two main stimulant medications for treatment are methylphenidate derivatives and amphetamine derivatives. Several Food and Drug Administration-approved nonstimulants are available.
- The potential consequences of untreated ADHD may progress to demoralization, poor self-esteem with resulting relationship difficulties, and impulsiveness leading to increased risk of substance abuse.

epidemiological data, diagnostic criteria, and evidence-based treatment options. Case examples at critical points emphasize clinical relevance.

ADHD: A Historical Perspective

In 493 B.C., Hippocrates documented perhaps the first known medical report related to present day ADHD by describing a condition in which patients had “... quickened responses to sensory experience, but also less tenaciousness because the soul moves on quickly to the next impression.” Interestingly, he considered the etiology stemmed from an overbalance of “fire over water” and prescribed dietary changes and exercise — a regimen that reverberates in some of the 2020 adjunct interventions for ADHD treatment.⁵

Two thousand years later, in 1798, prominent physician Sir Alexander Crichton published a book chapter titled “Attention and its Diseases,” describing a group of patients with abnormal inattention characterized by “the incapacity of attending with a necessary degree of constancy to one object.” He noted patients often were born with this condition, that it manifested during early years of life, and that it interfered with education, but often resolved or diminished with age.⁶

The 1800s gave birth to a range of descriptors and terminology regarding impulsive children with poor attention and behavioral problems. Prominent physicians on both sides of the Atlantic Ocean, including Benjamin Rush in the

United States, contributed to the case reports and literature. Interestingly, a movement toward compulsory education also gained traction during this time.⁷

One hundred years later, Sir George Frederic Still, known as the father of British pediatrics, delivered the Goulstonian lectures, often considered the starting point of the modern-day conceptualization of ADHD. He described a condition noted in children, characterized by poor attention, poor concentration, emotional lability, and behavioral problems and labeled this “an abnormal defect of moral control.”^{7,8}

Momentum grew in the 1900s toward recognizing, describing, and treating children with symptoms of inattention, hyperactivity, and impulsivity. In the early part of the century, Franz Kramer and Hans Pollnow, both German physicians, studied a series of children with extreme hyperactivity. Coining the term “hyperkinetic disease of infancy,” the two attempted to characterize the typical course and outcome of the disorder.^{7,8}

In 1937, Charles Bradley stumbled upon a treatment for many of these children. Bradley, in his role of medical director at a home for youth with neurologic and emotional disturbances, routinely performed pneumoencephalograms to look for abnormalities in the brains of the children. Following the procedure, children received the stimulant benzedrine to prevent subsequent headaches. Notably, behavior problems in many of the children resolved with the administration of the stimulant. From this inauspicious

beginning emerged a treatment for patients with ADHD. Over time, stimulant formulations have become more sophisticated, but the use of stimulant medication remains a primary treatment for ADHD even today, almost 100 years following Bradley’s discovery.^{7,8}

In the 1900s, evolving terms to describe ADHD captured the progressing conceptualization of this condition. An initial concept of “minimal brain dysfunction” was replaced in the 1968 DSM-2 by the more specific “hyperkinetic reaction of childhood” and finally “attention deficit disorder with and without hyperactivity” in the 1980 DSM-3. The DSM-4 in 1994 introduced the term in use today: ADHD.^{7,8}

Diagnostic Criteria and Epidemiology

As terminology regarding ADHD changed over time, diagnostic criteria evolved. However, the foundation of diagnosis remains unchanged: observation of behavior and functional impairment. Observational evidence often hinges on reports from multiple informants (patient, teachers, family); behavior in an office setting is not necessarily indicative of behavior at-large.

The current DSM-5 criteria state:⁹

1. Inattention: Six or more symptoms of inattention for children up to age 16 years; five or more for adolescents age 17 years and older and adults; symptoms of inattention have been present for at least six months, and are inappropriate for developmental level:

- a. Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or with other activities.
- b. Often has trouble holding attention on tasks or play activities.
- c. Often does not seem to listen when spoken to directly.
- d. Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., loses focus, side-tracked).
- e. Often has trouble organizing tasks and activities.
- f. Often avoids, dislikes, or is reluctant to do tasks that require mental effort over a long period of time (such as schoolwork or homework).

g. Often loses things necessary for tasks and activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones).

- h. Is often easily distracted.
- i. Is often forgetful in daily activities.

2. Hyperactivity and Impulsivity:

Six or more symptoms of hyperactivity-impulsivity for children up to age 16 years, or five or more for adolescents age 17 years and older and adults; symptoms of hyperactivity-impulsivity have been present for at least six months to an extent that is disruptive and inappropriate for the person's developmental level:

- a. Often fidgets with or taps hands or feet, or squirms in seat.
- b. Often leaves seat in situations when remaining seated is expected.
- c. Often runs about or climbs in situations where it is not appropriate (adolescents or adults may be limited to feeling restless).
- d. Often unable to play or take part in leisure activities quietly.
- e. Is often "on the go" acting as if "driven by a motor."
- f. Often talks excessively.
- g. Often blurts out an answer before a question has been completed.
- h. Often has trouble waiting their turn.
- i. Often interrupts or intrudes on others (e.g., butts into conversations or games).

Additionally, several symptoms must have started before age 12 years; several symptoms must be present in more than one setting; symptoms must interfere with functioning; and another mental illness cannot better explain the symptoms.

There are three main presentations of ADHD. As children grow and develop, presenting symptoms may shift. A recognition of this pattern drove the terminology to change from "subtype" in older editions of DSM to "presentation" in DSM-5.

Presentation of ADHD includes:

1. Combined presentation: meets criteria for both inattention and hyperactivity (numbers 1 and 2 of the DSM-5 criteria).
2. ADHD predominately hyperactive-impulsive meets criteria for hyperactivity and impulsivity.
3. ADHD predominately inattentive meets criteria for inattention.⁹

Given the changes in diagnostic criteria over the years, prevalence estimates vary. A 2015 meta-analysis estimated the worldwide prevalence among children younger than age 18 years at 7.2%. Currently, the Centers for Disease Control and Prevention (CDC) notes that data from a 2016 national survey of parents reveal 6.1 million of U.S. children ages 2 to 17 years have at some point been diagnosed with ADHD. This represents a drop from the 6.4 million children diagnosed in 2011, but a considerable increase from the 5.4 million children with such a diagnosis in 2007.¹⁰

Boys are about twice as likely as girls to be diagnosed with ADHD. Interestingly, boys also are more likely to display hyperactivity. The potential for disruption as a result of this symptom may be instrumental in recognizing ADHD in boys and may influence the likelihood of gender-based bias in diagnosis.¹¹

The median age of diagnosis for girls and boys is 6 years of age, with more severe cases usually diagnosed earlier and often before the age of 5 years.^{10,11}

ADHD may coexist with other psychiatric disorders; distinguishing symptoms and targeting intervention allows effective treatment. A disorder of behavior, such as oppositional defiant disorder (ODD) or a conduct disorder is comorbid with about 50% of ADHD diagnoses. Anxiety is both a frequent comorbid condition (in about 30% of cases) and an important diagnosis to consider as a differential, since anxiety often may present in a manner similar to ADHD.¹²

Learning disorders often co-occur with ADHD, although rates vary in published

studies. The confusion most likely reflects the difficulty distinguishing one condition from the other. Working with appropriate specialists to ferret out the etiology of learning problems typically enhances treatment efficacy.¹² The following case example illustrates some of these points.

Introducing M.

M., a healthy 5-year-old boy, presents with his mother after an administrator at his preschool told his mother they are having difficulty "meeting his needs." "He refuses to sit during circle time, hits at peers when waiting his turn, interrupts teachers during 'quiet time,' and attempts to run out of the building when frustrated," explains his mother. She notes these behaviors were present to a lesser extent last year, but his teacher was "very understanding." In addition, she says the school expects more this year, and he is dealing with changes in his schedule because of the recent divorce of his parents. At home, his mother adds, he has never sat long enough to watch an entire children's movie, listen to a story, or complete an age-appropriate project or chore. He has complained lately of stomachaches on school days.

M.'s difficulty meeting age-appropriate expectations for focus and attention both at home and at school meets a criterion for a diagnosis of ADHD: presenting as predominately hyperactive-inattentive. However, the stomachaches and running out of the building are symptoms that alert the provider to take a closer look and evaluate if anxiety is playing a role in this child's situation. His mother's remark about the recent divorce could be a factor. It also is appropriate to consider that anxiety may arise when a child perceives that he or she is unable to meet expectations. Intervention may need to address both the attentional issues as well as the possible anxiety. Additionally, screening for independent disorders that affect the ability to focus and follow auditory commands (such as hearing and auditory processing) is indicated.

Often, ADHD continues into teenage years. DSM-5 specifies that some of the presenting symptoms must start before the age of 12 years; this represents a significant change in thinking from previous DSM editions that used age 7 years as a cut-off point. This change is the result of recent findings that ADHD may emerge later in life than suspected previously

and/or may go unrecognized for a number of years.⁹

Introducing S.

S. comes in for a sports physical. A healthy 15-year-old 10th grader, quiet and eager to please, she states her grades have taken a nosedive this year. "Middle school was easy," she notes, "but high school is a different story. When we had 'real' school, I always forgot something – my gym uniform, cleats, violin music, even assignments. I was passing, but having trouble keeping up. Then coronavirus came, and everything went online. I was completely lost. My teachers would post assignments and I would start, then I would get on some random website, lose track of time, and never finish. Now we have a mixture of online and in classroom; I am even more confused. My dad says I get too distracted. My mother thinks I need to listen better."

S., with her forgetfulness, distractibility, and difficulty with follow-through, most likely meets a criterion for ADHD, presenting as predominately inattentive. However, it is not clear from her current history that symptoms began before the age of 12. She mentions that school used to be easier for her. It may be that the level of supervision built into earlier grade levels made up for her baseline disorganization and inattentiveness; it may be that her quiet nature kept her "under the radar" when it came to diagnosis; and it may be that more recent psychosocial factors are at play. Current research into late-onset ADHD (after the age of 12 years) indicates that this subtype may exist, but that there is typically an indication of a precursor in earlier years. Collateral information from a guardian and/or school personnel, and a history looking for evidence of earlier onset attention and focus problems, is necessary for a diagnosis.¹³

Persistence rate estimates of ADHD from childhood into adulthood vary widely, from a low of 14% to a high of 78%. This wide range is most likely explained by multiple variables, including poor standardization of diagnostic tools, type of informant (self-report vs. parent report) regarding history and current symptoms, and a generalized shift with maturity toward a more subtle presentation of symptoms, making adult ADHD more difficult to detect. However, recent

studies have pointed to risk factors associated with ADHD persistence. These include higher severity of ADHD symptoms in childhood, comorbid conduct disorder and/or depressive disorder, and parental mental health problems.^{13,14}

Introducing T.

T. is a 26-year-old first-year medical student with a stellar undergraduate academic history. He presents with frequent distractibility, restlessness, interrupting peers during class discussions, and difficulty remembering and completing assignments, along with a decline in grades during the academic year resulting in academic probation. The dean of the medical school has advised him to come in for a physical and to consider taking time off. His history reveals a diagnosis of ADHD with school accommodations (but no medication) as a preteen and depression during high school, treated successfully with nine months of citalopram and counseling. He wonders if depression is a factor again, but says, "It feels different this time." His mood is not particularly low, his appetite is unchanged, but his sleep patterns vary. A general physical and basic lab panels reveal no abnormalities. His family history is significant for ADHD in a sibling and cousin; depression in his mother; and no substance abuse, bipolar disorder, or suicides in close family members.

T. presents with symptoms suggestive of ADHD: presenting combined type. The history of an earlier diagnosis of ADHD and depression puts him in a higher risk category of continuing ADHD into adult years. Although he was able to manage without medication in earlier years, the higher academic demands he faces now may require intervention that is more intensive. Continuing to gather history (including symptoms of ADHD as a preteen) while evaluating for comorbid psychiatric diagnosis is a reasonable path.

Diagnostic Tools

ADHD remains a diagnosis reliant on documentation of behaviors aligned with DSM-5 criteria, supplemented with a comprehensive history and physical examination. History from prenatal years (where possible) and covering development, academic performance, biological, psychosocial, and environmental factors is useful for diagnostic purposes and to rule out conditions with overlapping

presenting symptoms, such as mood disorder. Obtaining a family history is relevant, since ADHD has a heritability estimate at above 75%.¹⁵

A detailed physical examination, paying attention to vital signs and looking for evidence of neurological impairment, as well as a mental status exam, aids diagnosis. The mental status exam may help confirm distractibility and/or hyperactivity, but also is useful to assess for the presence of any comorbid psychiatric conditions, such as anxiety or depression. Finally, the clinician may assess for conditions affecting hearing and vision, as well as suggestions of auditory processing and learning difficulties.^{15,16}

M., the 5-year-old about to lose his spot in preschool, tolerates a full physical examination. His vision and hearing screens are normal, as is the remainder of his exam, with the exception of moderate hyperactivity. He requires frequent reminders and redirection but seems eager to please. He clearly is distressed about school, noting, "I try to be good, but I keep being bad. Then mommy cries and daddy yells on the phone." Family history is significant for two paternal uncles with ADHD. His mother notes he has a hard time sleeping on school nights and that his father has noted the same. When asked, his mother thinks that school will keep him if there is a plan to address his behavior.

Teacher and parent behavior-rating scales have been used for assessment and monitoring of ADHD symptoms since the late 1960s. Table 1 contains examples of some commonly used scales and relevant details. Many clinicians ask parents and/or teachers to complete the scales at baseline and every three to six months during treatment. The adjustment of medication dose often is heavily reliant on results. Given the inherent subjectivity of these rating scales, input from multiple observers in multiple settings is useful to obtain a full picture of behavior and functioning.¹⁷

S., the 15-year-old in for a sports physical, has an unremarkable physical exam. Additional history reveals she has had trouble keeping organized at school and at home "as long as I can remember, but my parents used to remind me of what I needed for school, checked my assignments, and every night, helped me lay out what I needed for the next day." This year, S. explains, her parents decided she should "take the reins" and be

Table 1. Examples of ADHD Scales

Scale	Age Range	Website Information	Relevant Details
National Institute for Children's Health Quality Vanderbilt Assessment Scales	6 to 12 years	https://www.nichq.org/sites/default/files/resource-file/NICHQ_Vanderbilt_Assessment_Scales.pdf	Initial and follow-up scales available; parent- and teacher-specific forms
Conners Comprehensive Behavior Rating Scale	6 to 18 years; 8 to 18 years (self-report)	https://www.wpspublish.com/conners-3-conners-third-edition	Parent- and teacher-specific forms; self-report available; long and short forms
ADHD Rating Scale IV—Preschool Version	3 to 5 years	https://fliphtml5.com/xibq/ekgw	18-item form; gender-based; parent and teacher forms are the same

ADHD: attention deficit hyperactivity disorder

less dependent on them. “I was really excited to feel more independent,” says S., “but I just can’t figure out how — it’s like slogging through fog in my brain each day.” She is agreeable to bring Conners Comprehensive Behavior Rating Scale forms home and to school, and to have her parents present at her next appointment. She says, “Both my brothers and some of my boy cousins take medication for ADHD. I just always thought it was something that hit the boys in our family — they are loud and run around and I am not like that!”

In the world of “real-life” medical practice, having the time to collect and interpret all of this information can feel burdensome. It is helpful to remember that recognition and treatment of ADHD is not an emergency; taking several appointments or an extended appointment time to gather relevant information and make a careful diagnosis often pays off in the long-term care of the patient.^{15,16}

With the advent of electronic health records (EHRs), interest in using electronic communication to communicate is growing. There are multiple studies in the field of health information technology (HIT) looking toward interventions that increase ease of communication among caregivers and providers and assist in collecting and compiling ADHD-rating scales. In general, some of these are integrated into an existing EHR (such as the ADHD Care Assistant developed at Children’s Hospital of Philadelphia) and others are stand-alone software.^{15,18}

When T., the medical student, is asked about symptoms of ADHD leading to a diagnosis when he was younger, he says, “I think the teachers noticed that I finished my work easily, but I always forgot homework, I would never know when we were having tests, and I would get in trouble for blurting out answers. I went to the doctor and they gave me a computer test, and suddenly school let me use electronic devices to keep organized — I was one of the first in my school!” This organizational technique worked well until medical school, he explains, noting he still depends on his electronic calendar and notifications, but “it is obviously not enough.” A mental status exam reveals an anxious young man, appropriately worried about his situation, with no evidence of hypomania or depression and with a clear ability to problem-solve and discuss treatment options. He denies any illicit substance use and any misuse of prescription medication but notes he has started to drink at night when he cannot sleep. “I am just so worried about school,” he says. “I don’t want to disappoint my family. I started drinking a beer before bed, then it turned into two or more. My girlfriend made me get rid of all of it, and I know she is right.”

Diagnostic tools specific for adults are available, and studies looking toward evidence of clinical accuracy for adult scales and interviews are growing. Recent research points to the accuracy of DIVA 2.0 — a semi-structured interview for adults developed in the Netherlands. This interview covers diagnostic criteria aligned with the DSM-5 and specifically

looks for symptoms before the age of 12 years and current functional impairment.¹⁹ There also is suggestive evidence that self-rating measures, such as standardized checklists, can assist in diagnosing adult ADHD. The Adult ADHD Self-Report Scale Symptom Checklist (ASRS) frequently is used and available without charge. This checklist covers 18 behaviors often noted in patients with ADHD. Patients self-score each item on a spectrum ranging from “never” to “often.” Such scales are designed to take five to 10 minutes and can be completed easily in a clinic waiting area.²⁰

Neuropsychological testing has limited evidence for diagnostic usefulness. More often, this type of testing is used when the history is inconsistent, when there are significant concerns about a differential or comorbid psychiatric diagnosis, or when other factors are present, making diagnosis unclear. There is insufficient evidence for reliance on any objective assessment tools, including electroencephalogram (EEG) and/or neuroimaging. It bears repeating that diagnosis usually comes down to a history and physical exam, teacher and parent rating (or possibly self-rating scales for older teens and adults), and the presence of functional impairment in more than one setting in areas aligned with the DSM-5 criteria.^{15,16,21}

Treatment

ADHD treatment with stimulant medication and behavioral interventions

dates back more than 40 years. Hundreds of studies have confirmed the efficacy and safety of stimulant medication when taken at prescribed doses and monitored. Notably, these are controlled substances; the provider is on solid ground considering the risk of recreational diversion and/or misuse before prescribing. Side effects to consider include mild elevation of pulse and blood pressure, decreased appetite, headache, and sleep disturbance. Obtaining a cardiac history (personal and family) to look for cardiac risk factors, such as family history of sudden cardiac death or a history of prolonged QT, is appropriate. Patients with such risk factors need further evaluation before starting a course of stimulants.^{15,16,22}

A long-term follow-up study (the Multimodal Treatment of Attention Deficit Hyperactivity Disorder, or MTA) noted that children on two to three years of consistent moderate to high doses of stimulants had a decrease in growth velocity, translating to an expected 1 cm to 2 cm diminished adult height. This may be the result of the decrease in appetite, as well as other factors.²³

Hallucinations and psychotic symptoms are more unusual but clinically worrisome adverse effects of stimulants. These typically are self-limited and subside after stopping the stimulant.²⁴

The two main branches of stimulant medication used for ADHD are methylphenidate derivatives (such as Ritalin) and amphetamine derivatives (such as Adderall.) Table 2 lists some of the Food and Drug Administration (FDA)-approved formulations available today. Typically, a patient starts on a low dose, and then tapers to the most effective dose over subsequent weeks, with feedback from appropriate scales and informants. If side effects are significant and/or results are insufficient, a new trial with a stimulant with a different release mechanism or from a different category often is the next step. This “trial and error” method of treatment may be frustrating to patients; frequent communication is essential to determining the most effective treatment plan.²⁵

There are several FDA-approved non-stimulants for the treatment of ADHD: the norepinephrine reuptake inhibitor atomoxetine (Strattera) and the alpha-2 adrenergic agonists extended-release

guanfacine and extended-release clonidine. The effect size of these nonstimulants is less than the effect size of the stimulants (0.7 vs. 1.0), which means that, although the nonstimulants show some efficacy in treating ADHD, the results are less robust than when stimulant medications are used. Although atomoxetine is approved for use into adult years, the alpha-2 agents are not approved past age 18 years for the treatment of ADHD.²⁶

These nonstimulants have side effects as well, with significant gastrointestinal discomfort associated with atomoxetine (especially with dose increases) and, less commonly, a potential for emergence of suicidal thoughts. The alpha-agonists decrease blood pressure and pulse, causing somnolence, dry mouth, and bradycardia for some patients. Given a potential for rebound hypertension with sudden discontinuation of these agents, tapering the dosage rather than stopping abruptly is recommended. These agents tend to be particularly useful when there is a contraindication to stimulant use or when stimulants have been ineffective.^{15,16,26}

Nonpharmacologic Approaches to Treatment

Parents of children diagnosed with ADHD express numerous concerns about using pharmacologic agents, including questions about the long-term effect of chronic medication use in children, implications of using controlled substances in youth, cost factors, and efficacy limitations. Even the long-acting stimulants are time-limited in action, generally wearing off by late afternoon or early evening. Adults with ADHD share many of these same concerns.³⁹

One of the more popular areas of research looking at nonpharmacologic interventions for children with ADHD revolves around diet. Results are inconsistent for efficacy of many specific diets (ranging from ketogenic to gluten-free to low sugar), but there are anecdotal reports of children responding to dietary interventions. The “few foods” diet (FFD) is a stringent elimination diet used primarily in the Netherlands to help identify subgroups of children with ADHD who may respond to dietary intervention. Foods are significantly restricted for a few weeks. If symptoms improve, it is suspected that the child will respond to dietary intervention.

Foods are reintroduced slowly; if behaviors return, the “culprit food” is eliminated. Researchers in this area are looking at less cumbersome ways to identify a population more apt to respond to dietary control of ADHD symptoms.⁴⁰

In adults, mindfulness-based interventions and specific types of behavioral therapy show promise, but participant groups have not been randomized and numbers are too small to generalize results. Multimodal treatment with a team approach is a well-established approach when caring for children with ADHD, but there are not sufficient studies to either recommend or rule out usefulness for the adult population.²²

Clinical Practice Guidelines

Clinical practice guidelines for the treatment of ADHD in children ages 4 to 18 years, published by the American Academy of Pediatrics (AAP) in 2001 (and revised in 2011 and 2019), offer the primary care provider (PCP) a clear decision-making pathway when working with children with this diagnosis. AAP guidelines stress that ADHD should be recognized and treated as a chronic health condition, with a place in the medical home.¹⁶

Preschool (Ages 4 to 6 Years)

Parent training in behavior management (PTBM) and/or behavioral interventions within the classroom are the first-line of treatment. Typically, PTBM involves eight or more parent-training sessions, with parents practicing newly learned techniques of behavior intervention between sessions. Although young children may benefit from specific types of therapy (such as play therapy), there is no evidence that behavioral changes related to ADHD symptoms result from child-centered therapy. Studies are increasingly suggestive that training parents to address specific symptoms exhibited by children has significantly more effect on these behaviors.¹⁶

If PTBM and/or behavioral interventions within the classroom are unsuccessful and functional impairment continues, the risks and benefits of using the psychostimulant methylphenidate should be evaluated. These risks include that the

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Table 2. Some Common Stimulants Used for the Treatment of ADHD

Generic Name (Brand Name)	Type of Medication	Typical Duration of Action	Dose Range	Notes
Mixed amphetamine salts (Adderall) ²⁶	Amphetamine stimulant: short-acting	4 to 6 hours	2.5 mg daily to twice daily, up to 40 mg daily (usually in divided doses because of short length of action)	FDA-approved 3 to 6 years; not AAP recommended
Dextroamphetamine sulfate (Dexadrine) ²⁷	Amphetamine stimulant: short-acting	4 to 6 hours	2.5 mg daily to twice daily, up to 40 mg daily (usually in divided doses because of short length of action)	FDA-approved 3 to 6 years; not AAP recommended
Extended-release amphetamine (Adderall XR) ²⁸	Amphetamine stimulant: long-acting	8 to 10 hours	10 mg to 30 mg daily	Biphasic absorption with immediate and delayed release; may sprinkle
Extended-release amphetamine (Dexedrine Spansules) ²⁹	Amphetamine stimulant: long-acting	6 to 8 hours	5 mg to 30 mg daily or 5 mg to 15 mg twice daily	Some consider this an “intermediate release”
Lisdexamfetamine (Vyvanse) ³⁰	Amphetamine stimulant: long-acting	10 to 12 hours	10 mg to 70 mg (10 mg increments)	Dextroamphetamine prodrug — reduced potential for abuse; capsule may be sprinkled; chewable form
Methylphenidate (Methylin) ³¹	Methylphenidate stimulant: short-acting	3 to 5 hours	5 mg daily to 60 mg daily (often in divided doses)	Tablet, liquid, and chewable forms
Methylphenidate (Ritalin) ³²	Methylphenidate stimulant: short-acting	3 to 5 hours	5 mg daily to 60 mg daily (often in divided doses)	5 mg, 10 mg, and 20 mg tablets; may cut tablet for dose adjustment
Dexmethylphenidate (Focalin) ³³	Methylphenidate stimulant: short-acting	4 to 6 hours	2.5 mg twice daily to 10 mg twice daily	2.5 mg, 5 mg, and 10 mg tablets
Methylphenidate extended-release (Metadate CD or Ritalin LA) ^{34,32}	Methylphenidate stimulant: intermediate-acting	6 to 8 hours	2.5 mg twice daily to 10 mg twice daily	Immediate and extended release in capsule; may be sprinkled
Methylphenidate extended-release (Concerta) ³⁵	Methylphenidate stimulant: long-acting	10 to 12 hours	18 mg to 72 mg	Immediate and extended release in capsules
Methylphenidate extended-release (Daytrana) ³⁶	Methylphenidate stimulant: long-acting	11 to 12 hours	10 mg to 30 mg daily	Patch form, boxes of 30
Methylphenidate extended-release (Quillivant XR) ³⁷	Methylphenidate stimulant: long-acting	10 to 12 hours	20 mg to 60 mg	Liquid
Extended-Release Dexmethylphenidate (Focalin XR) ³⁸	Methylphenidate stimulant: long-acting	8 to 10 hours	5 mg to 40 mg	May be sprinkled

ADHD: attention deficit hyperactivity disorder; FDA: Food and Drug Administration; AAP: American Academy of Pediatrics

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long-term effect of this medication on the developing brain is not well studied. The maximum dose range in this age group is not established; start low and proceed slowly is the rule of thumb. Note that this is an off-label use of methylphenidate, since the level of evidence is not sufficient to meet FDA standards. On the other hand, amphetamine is FDA-approved for use in children younger than 6 years of age, but the AAP does not believe evidence is adequate to support the use of amphetamine as first-line treatment of ADHD in preschoolers.¹⁶

The mother and father of preschooler M. are agreeable to start a PTBM program. Unfortunately, the program does not start for three months. His parents are concerned that M. "needs something now" if he will be able to be maintained in his preschool. The ADHD rating scale (preschool version) from school indicates problems with focus, hyperactivity, and self-control. A written message on the form notes that his behaviors seem to be worse on days when he is transitioning between parents' homes. After discussing this with his parents, they agree to make M.'s schedule more consistent, to establish regular communication between school and both parents, and to make sure to praise M. when he has had positive interactions at school. The school as well is willing to set up a positive behavior program for M. All decide to re-evaluate after one month.

Elementary Through High School (Ages 6 to 18 Years)

For children in elementary and middle school diagnosed with ADHD, the AAP recommends a multipronged approach. This treatment strategy combines an FDA-approved medication (typically a stimulant medication) with PTBM and a behavioral plan within the classroom. For many youngsters with ADHD, the behavioral plan may include elements such as preferential seating, assistance with organization, and a quiet setting for tests. These interventions are usually school designed and driven but may be initiated when a PCP requests that a child be evaluated for a "504 plan."^{15,16}

A 504 plan reflects accommodations necessary for learning for a student with a specified disability or medical condition. This should be distinguished from an Individualized Education Plan

(IEP), which is more appropriate for children who require a specialized form of instruction.⁴¹ In the era of COVID-19, many children have migrated to a home learning environment. This may change the specific accommodations needed but does not change the need for accommodations.

High schoolers present some unique challenges when treating ADHD. The AAP highlights the utility of involving this age group in decision-making, including reviewing risks and benefits of medication, educating about controlled substances, and teaching self-assessment. As mentioned earlier, it is unusual for symptoms to develop after the age 12 years; if there is no suggestion of precursor symptoms, other diagnoses should be considered more strongly (including mood disorders and substance abuse).

The AAP recommends a multipronged approach for this age group as well, with FDA-approved medication and school-based behavioral interventions. PTBM is less useful at this age because of parent-teen interactions.¹⁶

Fifteen-year-old S. returns with her parents, who have completed the Conners Comprehensive Behavior Rating Scale form for parents. Two of her teachers have faxed Conner forms back to the PCP's office. Scores for inattentiveness and distractibility are significantly elevated. All show clinically relevant elevation of scores, reflecting difficulty with organization and distractibility. Subscales related to hyperactivity, defiance, aggression, and peer relations score in the "average" range. The subscale reflecting anxiety is mildly elevated.

Her parents agree with S. that she did better overall when they were helping with organization. However, they note that the current structure of her school and their own work commitments make this unrealistic going forward. They wonder if their own efforts at helping her in younger grades make it more difficult for her to function independently now. Her school is willing to work with her on building organizational skills and to give her tools to assist with staying focused during online learning. All are willing to consider a 504 plan based on helping build these skills.

S. is willing to try medication, "if it can help." With parental consent and after a review of medical history (including personal and family history of cardiac disease

and disorders of mental health), S. is started on lisdexamfetamine (Vyvanse), 20 mg daily. S. agrees to use online tools to self-monitor her level of distractibility. Her parents agree to email or call at the end of seven days to determine the need for a dose increase based on teacher reports, parental observation, and self-assessment by S. Her teachers and parents plan to email or fax follow-up Conner forms monthly to help with dose refinement. S. and her parents are educated about controlled substances and sign an agreement regarding use of such substances.

Agreements or contracts for controlled substances are common. Generally, these are one-page statements acknowledging that the patient is aware that the medication is controlled, that there is a potential for abuse, and outlining the process to obtain refills and/or report lost or stolen pills. Many EHRs have such forms embedded in the platform; sample forms also may be obtained online.⁴²

Many states mandate that providers prescribing these controlled substances check the prescription drug monitoring program (PDMP) to help track and follow prescription patterns for individual patients. Many EHRs link directly to state PDMPs, allowing a seamless integration with real-time prescription dispensing.⁴³

With fewer checks and balances on behavior, monitoring for overuse and/or potential misuse of stimulants becomes increasingly important as patients enter into independence and adulthood.

The AAP guidelines for treatment of ADHD are limited to ages 4 to 18 years.¹⁶ Research in treatment of ADHD in adults lags behind pediatric studies. However, in 2017, an international group of investigators conducted a meta-analysis covering 40 studies in this field to provide initial recommendations.²²

Conclusions from this meta-analysis reveal that pharmacologic agents are significantly more efficacious than placebo in the treatment of adults with ADHD, but less well tolerated. Stimulants were the most frequently studied ADHD medication, followed by atomoxetine. Although amphetamines seemed to be associated with a slightly more robust response, given the number of studies and participants, methylphenidate is recommended as the first-line agent of choice in this age group.²²

The recommendations are to monitor weight, heart rate, and blood pressure when treating with any stimulant medication.²²

The nonstimulant atomoxetine is recommended for patients unable to tolerate stimulant medication and/or for patients at risk of abusing these agents. This becomes particularly important in the college-age student, since this population has a rate of stimulant misuse of about 17%. Use of atomoxetine or the sustained-release form of stimulant medication, as well as careful follow-up and checking PDMP helps manage this risk.²²

Also stressed in this meta-analysis is the importance of having an adult informant (in addition to the patient) provide collateral history, especially if the patient was not diagnosed with ADHD in childhood, performing a careful history and physical exam, and examining for co-occurring mental health disorders, including substance use.²²

"I want to try a stimulant," says medical student T. "I never wanted to try meds before, but I think this may be my best shot to salvage my year." He has made an appointment at the university counseling center "for support and to see if they can help me figure out how to sleep," and signs a release to coordinate care. In addition, he reaches his father by phone during his appointment and his father confirms T.'s early history of ADHD diagnosis. After checking the PDMP and reviewing his controlled substance agreement, T. is started on methylphenidate ER 18 mg daily, with instructions to taper up to 36 mg after seven days and return for a re-check in two to three weeks. He agrees to complete an adult ADHD self-monitoring scale weekly and email the results to the clinic. He is cautioned to stop medication if his insomnia worsens, not to use alcohol to help with sleep, and to pursue counseling and discuss techniques to aid sleep. He is clear that the medication most likely is only one part of a solution, stating, "I used to think I was lucky that I didn't have to study. Now I need to learn HOW to study."

Given that T. is at risk of academic failure, an immediate intervention is reasonable. Choosing a long-acting stimulant helps reduce the risk of diversion and abuse. Writing prescriptions for a limited quantity of medication initially aids in developing a treatment alliance (to determine the most effective dose) and

encourages T. to become more self-aware. Given the history of depression and the self-report of using alcohol for sleep, establishing a treatment team approach with the counselor is warranted.

The potential consequences of untreated ADHD, as documented in multiple studies, may progress from academic difficulties to underemployment to demoralization, poor self-esteem, and consequent relationship difficulties. Impulsiveness leads to elevated risk of substance abuse. A comprehensive treatment strategy appears to be the most effective mechanism to mitigate these outcomes.^{22,44}

Conclusion

ADHD is a complicated neurodevelopmental disorder, beginning in childhood and often extending into adult years, with a presentation strongly influenced by intertwining internal and external factors. Patients with ADHD present at a variety of ages and developmental stages. What almost all have in common is that they present with functional impairment that is not better explained by a diagnosis other than ADHD. Notably, personality, parental style, and societal expectations all play a role in dysfunction caused by symptoms of this disorder, making individualization of treatment a priority.

The AAP strongly recommends adopting a treatment model used in management of other chronic conditions, such as asthma or diabetes. In this way, patients and caregivers become aware of the need for monitoring and controlling symptoms throughout a lifetime.¹⁶

The DSM-5 gives straightforward diagnostic criteria for ADHD. However, diagnosing and treating rarely are straightforward. ADHD often is comorbid with other disorders of mental health and with learning disorders; understanding and ferreting these out is essential for a targeted and effective treatment. Since this is a clinical disorder based on observation of specific behaviors, a comprehensive history (often with input from outside sources) and physical exam are the best diagnostic tools available.

There is a shortage of access to mental health clinicians in the United States. National survey data from 2016 point to more than 5 million children between

the ages of 2 and 17 years diagnosed with ADHD. Given these numbers, it is inevitable that the center of care for many of these individuals will be in the office of the PCP. Understanding the course of this chronic condition and being aware of the latest recommendations for diagnosis and treatment allow the PCP to collaborate effectively with patients and families in the management of ADHD.

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1. Attention deficit hyperactivity disorder (ADHD):
 - a. is one of the most common neurodevelopmental disorders of childhood; symptoms appear by age 7 years and usually disappear by maturity or young adulthood.
 - b. is a neurodevelopmental disorder of childhood occurring in about 1% of children; symptoms peak before age 12 years and, for the most part, fade by adulthood.
 - c. is one of the most common neurodevelopmental disorders of childhood; symptoms appear by age 12 years and, in many cases, continue into adult years.
 - d. is a neurodevelopmental disorder of childhood occurring in about 1% of children; symptoms appear by age 7 years and fade by adulthood.
2. Which of the following is required for the diagnosis of ADHD?
 - a. A comprehensive history and physical exam, exclusion of conditions that may better account for symptoms, and data showing that symptoms are present in more than one setting and cause functional impairment
 - b. A comprehensive history and physical exam, psychological testing, and exclusion of learning disorders
 - c. A comprehensive history and physical exam, psychological testing, and exclusion of emotional disorders
 - d. A comprehensive history and physical exam, psychological testing, and parenting assessment in younger children
3. Which of the following risk factors are associated with persistence of ADHD into adulthood?
 - a. Higher severity of ADHD symptoms and substance abuse before age 18 years
 - b. Earlier diagnosis of ADHD and substance abuse before age 18 years
 - c. Higher severity of ADHD symptoms and conduct disorder or depression before age 18 years

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- d. Substance abuse, bipolar disorder, or anxiety before age 18 years
4. Teacher and parent behavior rating scales:
 - a. are useful to help confirm ADHD diagnosis, but are rarely helpful in monitoring followup because of lack of standardization.
 - b. are available for specific age groups and useful for monitoring symptom response.
 - c. are used frequently during elementary school years to help assess response to treatment, but are less useful above this age, since they are not well standardized.
 - d. are used primarily to document baseline symptoms in ages 12 years and older.
 5. Which of the following is appropriate first-line treatment of ADHD in children younger than age 6 years?
 - a. Cautious use of methylphenidate, if symptoms are severe
 - b. Appropriate school placement (such as a special-needs preschool) and play therapy
 - c. Cautious use of a nonstimulant, if symptoms are severe
 - d. Parent training in behavior management (PTBM) and classroom behavioral interventions
 6. Treatment of elementary school children with ADHD includes which of the following?
 - a. A multipronged approach with stimulant medication, PTBM, and classroom interventions
 - b. A multipronged approach with nonstimulant medication, therapy, and an individualized education plan (IEP)
 - c. A multipronged approach with stimulant medication, therapy, and an IEP
 - d. A multipronged approach with nonstimulant medication, PTBM, and therapy
 7. Treatment of high school students with ADHD includes which of the following?
 - a. A multipronged approach with nonstimulant medication, PTBM, and classroom intervention
 - b. A teen-centered approach with a focus on mindfulness and study skills before medication
 - c. A multipronged approach with teen involvement, stimulant medication, and classroom intervention
 - d. A teen-centered approach with a focus on study skills, social skills, and emotional regulation before medication
 8. Treatment of adults with ADHD:
 - a. is not recommended — there is no evidence that ADHD is a problem for adults.
 - b. involves cautious use of stimulant or nonstimulant medication and monitoring.
 - c. is recommended only in extreme cases, since ADHD rarely affects adults.
 - d. is contraindicated if the patient does not have a history of prior ADHD treatment.

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