

Attention-Deficit/Hyperactivity Disorder in Adults: Clinical Information for Primary Care Physicians

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Focus Points

- This article describes the prevalence of attention-deficit/hyperactivity disorder (ADHD) in adults and reviews adult ADHD diagnostic criteria.
- The clinical impact of adult ADHD is discussed in detail.
- Comorbid psychiatric conditions that may complicate treatment of ADHD in adults are described.
- Current available treatment options for adults with ADHD are discussed and explained.

Abstract

This article is intended to help the primary care physician (PCP) recognize attention-deficit/hyperactivity disorder (ADHD) in adults and to assess treatment options. Although ADHD was originally considered a childhood disorder, there is now growing recognition that most individuals diagnosed in childhood continue to have significant symptoms throughout their life cycle. ADHD may impair adults socially and occupationally and is associated with behaviors that place them at increased medical risk. Accurate diagnosis remains a challenge. While the media and medical literature are now flooded with information about how to treat ADHD in adults, there is relatively little information about deciding whom and when to treat. This article seeks to provide practical guidelines and advice on how PCPs can detect ADHD in their patients and make prudent treatment decisions.

Introduction

Fidgety Phil,
He won't sit still;
He wriggles,
And giggles,
And then, I declare,
Swings backwards and forwards
And tilts up his chair..

The poem "Fidgety Philip," written in 1844 and printed in *Lancet* in 1902,¹ is among the first accounts of childhood attention-deficit/hyperactivity disorder (ADHD) in the medical literature. Physicians have been diagnosing childhood ADHD and treating it with stimulants for more than half a century. However, in the past few decades, the notion of the disorder has been radically reconceptualized, the understanding of its neuroanatomical and neurochemical basis has been

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expanded, and new treatment options have been developed.

For example, there is now growing recognition that most individuals diagnosed with ADHD in childhood continue to have significant symptoms throughout their life cycle. ADHD may impair adults socially and occupationally and is associated with behaviors that place them at increased medical risk. Although accurate diagnosis of adult ADHD remains a challenge, this article seeks to provide practical guidelines and advice on how primary care physicians (PCPs) can detect ADHD in their patients and make prudent treatment decisions.

What Is ADHD?

ADHD is a label for a heterogeneous group of genetically transmitted neurobiologic dysfunctions that hinder the ability of affected individuals to regulate attention, motor behavior, impulsivity, emotional expression, and judicious application of higher-order executive cognitive functions. ADHD was originally categorized as a childhood disorder, with emphasis generally placed on symptoms of hyperactivity rather than inattention (as reflected by early labels for the disorder, such as “hyperkinetic reaction of childhood”).² It has been increasingly appreciated, however, that ADHD is not only one of the most common childhood psychiatric, learning, or behavioral problems, affecting approximately 3% to 7% of children,³ but one which commonly persists into adulthood.⁴ Approximately one third to two thirds of individuals with childhood ADHD continue to have ADHD as adults. An even larger number of adults no longer meet full criteria for the disorder but continue to experience significant functional impairment and distress due to the persistence of some ADHD symptoms from childhood.⁵⁻⁷ As individuals with ADHD mature and adapt, symptoms of motor hyperactivity often diminish or take less noticeable forms. However, as the child becomes independent and the ability to regulate attention takes on an increasingly important role, deficits in this area may become more apparent.

What Is Adult ADHD?

Adult ADHD is generally believed to be a continuation of the childhood disorder.⁸ Of adults who had childhood ADHD, 50% to 80% no longer meet full *Diagnostic and Statistical Manual of*

Mental Disorders, Fourth Edition (*DSM-IV*),⁹ criteria for the disorder, but continue to show some ADHD symptoms that cause impairment.^{7,10}

Adult ADHD has significant clinical overlap with childhood ADHD. Adults respond to the same medications as do children with ADHD.¹¹⁻¹³ Adults and children with ADHD also have similar patterns of comorbid psychiatric disorders and similar characteristics according to findings in molecular genetic and neuroimaging research studies.¹⁴⁻¹⁶ By definition, ADHD begins in childhood, although precortical growth during adolescence, social maturation, and the ability to build compensatory mechanisms into the external environment may create a different presentation in adults and may account for the apparent “burn out” of some symptoms.

In the 1950s, hyperactivity was considered the core feature of ADHD and the disorder was mainly diagnosed in boys. At that time, ADHD was thought to remit by adulthood, in part because the hyperactivity and impulsivity of ADHD does indeed typically decrease.⁷ Although there has been growing awareness that ADHD involves attentional deficits as well as motor hyperactivity, boys are still diagnosed with ADHD four times more frequently than girls. This may be at least partially due to referral bias, since the impulsive and disruptive behaviors that often lead teachers to refer children to treatment are much more common in boys with ADHD than in girls with ADHD.¹⁶

Both the inattentive and the impulsive behaviors associated with ADHD can place affected adults at medical risk. Young adults with ADHD have been reported to have more sexual partners, to be less likely to use contraception and have safe sex, and to be at higher risk for sexually transmitted diseases than comparison groups.¹⁷ Adults with ADHD are more likely to abuse alcohol or drugs^{5,18,19} and to smoke cigarettes than are control populations.^{20,21} They are more likely to exceed the speed limit when driving, to have their driver's licenses suspended, and to have motor vehicle accidents.^{19,22}

Public awareness of ADHD has been growing for the past 2 decades. In the 1980s, two national advocacy organizations—Children and Adults with Attention-Deficit/Hyperactivity Disorder and the Attention-Deficit

Disorder Association—began holding annual meetings, increasing consumer awareness of ADHD and its treatment. In 1991, the United States Department of Education specifically recognized that ADHD was a condition that could allow children to become eligible for special education services. This educational reform may have increased the flow of children into treatment. Since the 1990s, there has been a documented dramatic increase in the number of patients presenting for treatment of ADHD and receiving medication.²³

With the increased recent media coverage of adult ADHD, more patients are requesting treatment. However, although many self-referred individuals have concentration and attention problems, they may not actually have ADHD.²⁴ The media and medical literature are now flooded with information about how to treat ADHD in adults, but not with information about discriminating ADHD from overlapping problems, deciding who to treat, and deciding when to treat. Given the recent explosion of interest in adult ADHD and the increase in treatment options, this article aims to provide practical guidelines and advice on how PCPs can accurately detect ADHD and make prudent decisions at every stage of the evaluation and treatment process.

ADHD and the Brain Executive Cognitive Functions and ADHD

Structural and functional studies associate ADHD with areas of the brain that conduct executive functions, which allow individuals to organize, prioritize, and integrate cognitive activity from moment to moment. These executive functions include self-monitoring, decision making, impulse control, organization and planning, and working memory—functions primarily controlled by the prefrontal cortex and its connections (ie, the basal ganglia, thalamus, and cerebellum).²⁵ Positron emission tomography (PET) scans and magnetic resonance imaging studies of adults with ADHD consistently point to involvement of the frontal lobes, basal ganglia, corpus callosum, and cerebellum.¹⁵

Typically, individuals with ADHD are inconsistent or unreliable in their ability to concentrate, rather than simply unable to concentrate. Most people with

ADHD can concentrate well in situations that interest them, but have trouble maintaining concentration if they are bored or distracted by more exciting internal or external stimuli. Conversely, they can have difficulty concentrating and attending to a task if they are aroused emotionally. In addition, some individuals with ADHD have difficulty moving from a task in which they are absorbed to refocus on new tasks.

This clinical picture of inconsistent attentiveness, impulse control, and activity level can be coherently understood using a conceptual model in which ADHD symptoms are viewed as manifestations of a core disturbance in the executive functioning of the brain.²⁶⁻²⁸ According to this model, as summarized by Gallagher and Blader,²⁸ ADHD-associated problems with behavioral control and management are not attributable to an inability to attend or to control actions, but rather to a decreased ability in the executive tasks of deploying, sustaining, and shifting attention, and from disturbances in determining the timing and ordering actions. Hyperactivity, according to this model, is not the result of excessive action, but a disturbance in the executive task of controlling arousal and level of activation.²⁸

Neurobiology of ADHD

Adults with histories of hyperactivity in childhood whose ADHD symptoms have persisted into adulthood have shown reduced volume and decreased metabolism in the prefrontal cortex and premotor areas. Brain PET scans have shown that when these adults engage in decision making, different neural circuits are engaged than in the brains of control subjects.²⁹⁻³⁰

Animal studies have implicated impaired use of dopamine and norepinephrine in the pathophysiology of behaviors analogous to ADHD. Clinically, nearly all medications that reduce ADHD symptoms increase available dopamine in the brain.³⁰ PET scan data in adults with ADHD have shown dose-dependent methylphenidate (MPH) inhibition of dopamine transporters in the brain. Therapeutic doses of MPH have been shown to occupy >50% of dopamine transporters, with time-to-peak uptake of brain dopamine correlating well with peak behavioral effects.³¹ Deficits in cholin-

ergic nicotinic receptors, dopamine and norepinephrine receptors and transporters, and the genes governing them have also been implicated,³² but patterns of genetic transmission remain inexact. Adoption, family, and twin studies support the concept that ADHD is highly heritable.³³⁻³⁵

Clinical Presentation of Adults with ADHD

Many adults with ADHD “grow out of” hyperactive symptoms or learn to adapt to them. The majority who remain symptomatic into adulthood have a combination of inattentive and impulsive/hyperactive symptoms.³⁶ They appear to have fewer hyperactive symptoms, a more even gender distribution, and greater genetic loading for the disorder than children. It is possible that those whose symptoms persist into adulthood have a more severe and heritable form of the disorder than those whose symptoms remit in adulthood.³⁴

More than half of adults with ADHD also have other psychiatric diagnoses,¹⁶ and many present with chief complaints which could be attributable to either ADHD or coexisting psychiatric disorders. Psychiatric conditions which frequently co-occur with ADHD include bipolar disorder, depression, anxiety disorders, substance abuse, antisocial personality disorder, and oppositional defiant disorder.⁸ The presence of overlapping psychiatric symptoms challenges the clinician with the task of distinguishing between ADHD, other psychiatric disorders, and the combination of ADHD and other disorders. Attention to differential diagnosis is critical to ensure that undetected psychiatric disorders, such as hypomania, cocaine abuse, or severe anxiety, are not misdiagnosed as ADHD. Complex presentation is the rule, not the exception.

Although it is difficult for PCPs to identify ADHD in adults, frequent complaints of adults seeking evaluation for ADHD commonly include symptoms related to inattention, such as difficulty initiating, shifting, sustaining, and refocusing attention; difficulty utilizing working memory and accessing recall (evidenced by, for example, chronically losing belongings); impaired ability to inhibit the processing of irrelevant information, which may result in apparently slow processing speed and concentra-

tion problems; and difficulty establishing and maintaining a routine. Other symptoms of inattention include disorganization, problems initiating and completing projects; poor time management and time estimation; and difficulty prioritizing and deciding when and how actions should be sequenced (Table 1).³

Adults with ADHD may also experience symptoms related to impulsivity or hyperactivity, such as interrupting or intruding; fidgeting; difficulty waiting turn, being inactive, or tolerating low stimulation; irritability and low frustration tolerance; reckless driving; and a subjective sense of inner restlessness or “being driven” (Table 1).³

Cumulatively, these problems may lead to significant social and occupational impairment. Individuals may report that they are unable to perform at work and school at the level that would be expected given their competence or intelligence; they may have difficulty finding or keeping jobs. Interpersonal problems, depression, and risk-taking behavior patterns, which increase their chances of illness and injury, are also common.^{17,26,36}

Diagnostic Evaluation of Adult ADHD

Accurate diagnosis of adult ADHD remains a challenge. The disorder is underrecognized and underdiagnosed by some clinicians, and overdiagnosed by others. There are no objective biological tests to diagnose ADHD and neuropsychological testing has been shown to have limited predictive validity in distinguishing ADHD from other psychiatric or neurological conditions.^{27,37,38} The diagnosis of ADHD is made through clinical history, using diagnostic criteria that are, to some extent, subjective and dimensional.

The *DSM-IV* remains the most widely accepted standard for diagnosing psychiatric disorders.⁹ With some modifications to allow for differences in adult and childhood presentations, *DSM-IV* criteria can be used to diagnose ADHD in adults. In the *DSM-IV*, ADHD is divided into three subtypes—predominantly hyperactive-impulsive ADHD, predominantly inattentive ADHD, and the combined subtype. Table 2 displays prevalence rates of these subtypes in clinically referred children and adults.^{3,36} In order to make a diagnosis of ADHD, there must be a his-

tory dating to childhood of at least six symptoms of inattention or at least six symptoms of hyperactivity/impulsivity, which cause clinically significant impairment in social, academic, or occupational functioning. There must also be clear evidence of clinically significant impairment in at least two settings, including social, academic, or occupational functioning.

Once the PCP suspects that a patient may have ADHD, he or she can further confirm the diagnosis by gathering information from sources other than the patient. Self-report and collateral ADHD rating scales, while not sufficient to establish a diagnosis, can provide additional information and serve as a baseline to monitor change over time. School reports, if available, and

information about whether other family members have been diagnosed with ADHD, are also valuable.

Rating scales, such as the Wender Utah Rating Scale (WURS),³⁹ the Brown Attention-Deficit Disorder (ADD) Rating Scale for Adults,⁴⁰ the ADHD Rating Scale-IV,⁴¹ the World Health Organization Adult ADHD Self-Report Scale-v1.1 Symptom Checklist,⁴² and the Conners' Adult ADHD Rating Scales (CAARS)⁴³ can be completed by patients and significant others (eg, family, peers, colleagues). These instruments are time efficient and increase the clinician's access to independent sources of information, including data about the patient's early childhood.

The WURS is a validated scale designed to diagnose childhood ADHD retrospectively.³⁹ The Brown ADD Scale⁴⁰ is a validated scale focusing on the executive functioning aspects of cognition that are associated with ADHD. It has standardized and validated clinician and self-report forms. The ADHD Rating Scale-IV⁴¹ rates symptoms using a four-point severity scale. It is based on the *DSM-IV* and assesses both hyperactive/impulsive symptoms and inattentive symptoms.

One problem with the description of ADHD in the *DSM-IV* and in instruments based on the *DSM-IV* is that ADHD is depicted in childhood, in the context of school and play. There are some relatively recent instruments, however, which describe ADHD symptoms in language that reflects adult contexts. One such instrument is the World Health Organization Adult ADHD Self-Report Scale-v1.1 Symptom Checklist.⁴²

The CAARS⁴³ also attempt to adapt descriptive language to the challenges of adulthood. The CAARS are available in both self-report and observer versions (eg, for completion by a spouse or parent) in three lengths—screening, short, and long. The CAARS assess both the severity and the frequency of symptoms. Validated clinician-administered and self-rated versions are available.

Treatment Issues

Why Do Adults Seek Treatment?

Some adults who seek treatment for ADHD have had beneficial treatment as children and may request continuing or restarting medication. Others recognize ADHD symptoms in them-

Table 1
DSM-IV-TR Core Symptoms of ADHD*

Symptoms of Inattention	Symptoms of Hyperactivity/Impulsivity
<i>The inattentive individual often:</i>	<i>The hyperactive individual often:</i>
Fails to attend to details or makes careless mistakes.	Fidgets with hands or feet or squirms in seat.
Has difficulty sustaining attention in tasks.	Leaves seat in situations in which it is inappropriate or has subjective feelings of restlessness.
Does not listen when spoken to directly.	Runs or climbs excessively in situations in which it is inappropriate or has subjective feelings of restlessness.
Does not follow through on instructions and fails to finish projects, etc.	Has difficulty engaging in leisure activities quietly.
Has difficulty organizing tasks and activities.	Is "on the go" or acts as if "driven by a motor."
Avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort.	Talks excessively.
Loses things necessary for tasks or activities.	<i>The impulsive individual often:</i>
Is distracted by extraneous stimuli.	Blurts out answers before questions have been completed.
Is forgetful in daily activities.	Has difficulty awaiting his or her turn.

* Language adapted for adults from *DSM-IV-TR*.

DSM-IV-TR=*Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition Text Revision; ADHD=attention-deficit/hyperactivity disorder.

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Table 2
ADHD Subtypes^{3,36}

ADHD Subtypes	Prevalence in Clinically Referred Children (%)	Prevalence in Clinically Referred Adults (%)
ADHD, Predominantly Inattentive Type (≥6 inattentive symptoms*)	25–30	35–40
ADHD, Predominantly Hyperactive-Impulsive Type (≥6 hyperactive-impulsive symptoms*)	10–20	<5
ADHD, Combined Type (≥6 inattentive and 6 hyperactive-impulsive symptoms)	>50	>50

* Summarized and adapted from *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition Text Revision.

ADHD=attention-deficit/hyperactivity disorder.

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selves after their children have been diagnosed and treated. Or, they may not know their diagnosis, but will present with a history of poor scholastic or job performance and difficulty planning and completing tasks. They may have difficulty following directions or remembering verbal instructions. As a result, intellectually capable individuals with ADHD may consistently fail to meet career or academic expectations. In addition, impulsivity, difficulty controlling angry outbursts, and inability to listen attentively to others may cause significant interpersonal problems. In some cases, friends and family may convince the adult with ADHD to seek treatment because they can no longer tolerate his or her symptoms.

Finally, some individuals may claim to have ADHD to obtain secondary gain. The potential for secondary gain may motivate patients to misrepresent themselves (deliberately or subconsciously) to clinicians. This is one reason that clinicians may be particularly concerned about relying on patients' self-report. Examples of secondary gain include being allowed extra time on tests and work assignments or gaining access to stimulants for recreational use, performance enhancement or, in some cases, simply to sell illegally. They might also view an ADHD diagnosis as an explanation or excuse for poor achievement or procrastination.

Unfortunately, there is no gold standard to quantify an individual's place on the attention-activity continuum and there is no clear boundary differentiating normal from abnormal attentiveness or activity. The inattentiveness of ADHD must be discriminated from inattentiveness due to other factors, such as sleep deprivation, environmental distraction, medication side effects, medical disorders, other psychiatric disorders, or substance abuse. The inconsistent performance and attention of adults with ADHD is often simply but inaccurately attributed to poor motivation and laziness or to oppositional, obsessive, argumentative, or passive-aggressive behavior. Brain scans may at some future date help to discriminate the inattention of ADHD from inattention of other etiologies; however, at present they are not sufficiently specific to be used diagnostically.³⁵

PCPs may be able to understand the inconsistencies of ADHD on a more

intuitive level by considering the normal changes in attention that adults experience from sleep deprivation. Even when sleep deprived, most people can sustain rapt attention at an exciting event (eg, an eagerly anticipated sports event or rock concert), but on the boring drive home, attention to traffic may be compromised despite great effort. The fluctuating attention of sleep-deprived adults resembles the typical experience of those with ADHD.

To Treat or Not to Treat?

Given the degree of uncertainty about the threshold for a diagnosis of adult ADHD and the complexity of identifying ADHD in many patients, how can a PCP decide who to actually treat for ADHD? As with any other medical condition, the PCP must weigh the risks and benefits of treating against the risks and benefits of not treating the illness. Many factors influence whether to recommend treatment to patients and which types of treatment to recommend.

The following questions are important to address in the decision-making process: How much suffering and dysfunction are ADHD symptoms causing in the patient's life? Are ADHD symptoms compromising the patient's work and social functioning? Are they contributing to the patient's failure to achieve specific life goals? Do ADHD symptoms cause the patient to expend disproportionate efforts to achieve socially appropriate life goals? Is the ADHD resulting in significant suffering of other individuals, creating significant relationship or parenting problems, or creating job instability due to difficulties with coworkers or supervisors? And finally, have the symptoms of ADHD significantly increased other health risks (ie, sexual impulsivity, risky driving, or substance abuse)?

The consequences of not treating adult ADHD can be serious and, in some cases, devastating for patients and their families. Adults with ADHD have more educational and job setbacks, delinquency, car accidents, license suspensions,^{19,44,45} and have a more extensive history of illegal drug use^{5,19} and thefts and arrests^{45,46} than controls. The prevalence of ADHD in a population of prisoners has been reported to far exceed its prevalence in the general public.⁴⁶ In the emotional arena, adults with ADHD report sig-

nificantly more psychological distress, interpersonal problems,¹⁹ marital problems,⁴⁵ and divorce⁴⁵ than control subjects. Chronic forgetfulness, irritability, lateness, disorganization, and impulsivity can have serious negative social consequences.

The effect of ADHD on family relationships and parenting can be devastating. When both a parent and child have ADHD, there are difficult challenges for each, since an impulsive and disorganized parent is likely to find it particularly challenging to meet the child's needs for structure and consistency. It is encouraging to note, however, that adults with ADHD who were treated with MPH experienced increased satisfaction with relationships, leisure activities, mood, and overall well being, as well as improvement in core ADHD symptoms, according to preliminary study results.⁴⁷

Not every adult with ADHD requires treatment. Some people develop adequate adaptive compensatory tools. Others have environments that allow them to compensate, such as significant others or staff who help keep them organized. Some succeed in situations where externally driven specific assignment deadlines, meetings, or exams assist them by structuring their time and activities, but they may flounder later when required to independently initiate tasks and set deadlines. In contrast, others may function well when they are in an environment without constraints or artificial distractions.

The need to treat adult ADHD must be considered in a psychosocial context for each individual. People with ADHD may be able to fulfill their full occupational and personal potential if their jobs are limited to working on a single task in a structured setting. But ADHD symptoms can be more damaging if affected individuals are expected to juggle complicated personal and professional meeting schedules, make quick and accurate decisions, handle large amounts of information under rapidly changing conditions, assess complex interpersonal signals, and accurately set priorities. For example, the bright professional with ADHD who must rapidly read technical materials, dissect the essentials of these materials, and reorganize information from multiple sources into a new document may be unable to begin. The

engaging and energetic salesperson may consistently fail and be “a day late and a dollar short” because he is unable to organize his sales schedule and effectively distribute his products to clients in a timely manner.

Treatment Options

The paradigm of the biopsychosocial treatment model is a helpful guide to clinicians for understanding the levels at which ADHD treatment may occur.

Biological Treatment Options

Despite claims to the contrary, dietary manipulations, such as sugar restriction,⁴⁸ have not been proven helpful in the treatment of ADHD. Pharmacotherapy has been the most effective cornerstone of ADHD treatment for decades. Stimulants, with their diffuse dopaminergic and noradrenergic release properties, have been first-line treatments for childhood ADHD since the early 1930s. The choice of a particular medication trial for a particular patient should be based on efficacy data, side effects, addiction history, and comorbid diagnoses. However, there is no reliable guidance for how to choose among different stimulants (ie, for an initial trial). If a biological relative has responded well to a particular medication, it might be considered a reasonable choice for an initial trial. Otherwise, medication choice is in part trial and error.

First-Line Medications: Medications with Demonstrated Efficacy in Treating ADHD

Psychostimulants. Psychostimulants, including MPH and amphetamine, have been studied in hundreds of clinical trials for over 50 years and are Food and Drug Administration-approved for the treatment of ADHD. Most studies report that stimulant treatment in children results in approximately 70% showing significant improvement in core behavioral symptoms and in at least a subset of associated impairments.^{49,50} Overall efficacy rates have been generally reported to be similar in adults, but there have been fewer controlled studies and some variability in results.^{13,51}

It is recommended that the prescriber first begin a medication trial with a short-acting stimulant. Short-acting stimulants are easier to titrate up, and in the event of an adverse reaction, may reduce the duration of the

patient's discomfort. However, once tolerability and optimal dosage are established, extended-release medications are recommended for maintenance treatment. Their advantages include easier compliance with the medication regimen and fewer mood swings in response to rapid changes in medication level. If one medication trial fails due to side effects or lack of efficacy, additional trials with other medications are recommended. Individuals who respond to one stimulant may respond differently to another, both in terms of effectiveness and emergent side effects.

Common side effects of stimulants include emotional and behavioral lability, increased anger (sometimes as a rebound effect), mild increase in pulse and blood pressure, insomnia, and appetite suppression. Potentially serious but rare side effects include hypertension, arrhythmias, worsening of tics, and psychosis. Stimulants are generally contraindicated in patients with a history of psychosis, thyrotoxicosis, tachyarrhythmias, severe hypertension, or angina. They should be used with extreme caution in patients with a history of anorexia nervosa or tics. Their safety is not established in pregnancy. Before prescribing any of the medications discussed, the clinician is urged to read in detail about side effects, contraindications, and medication interactions.

The classic treatments for ADHD, MPH and amphetamines, increase extracellular levels of dopamine in the brain; it is through this action (as well as noradrenergic effects) that improvements in attention and performance are thought to be mediated. However, concern has arisen regarding the potential abuse of MPH because of its similarity in neurochemical effect (increasing extracellular dopamine) to drugs of abuse, such as cocaine. MPH and cocaine have a similar mechanism of action in that they block the dopamine transporter, leading to a rise in dopamine levels in cortical and subcortical areas of the brain.

Swanson and Volkow,^{52,53} in a series of studies and reviews, have sought to elucidate the similarities and differences between MPH and cocaine in terms of their effect on dopamine transporter blockade and potential for

producing a “reinforcing high.” Their work helps clarify the factors that are important in determining the potential for abuse of methylphenidate. They found that the reinforcing effects of MPH are strongly tied to the rapid change in brain concentrations that occurs with intravenous (IV) administration of MPH and in that context may be comparable to drugs of abuse such as cocaine; however, when administered orally, even at equivalent rates of receptor binding (as compared with IV administration), a reinforcing high was rarely seen with MPH.

Atomoxetine. Atomoxetine is a norepinephrine transporter inhibitor which is FDA-approved for the treatment of ADHD in both children and adults. It is the first medication specifically for ADHD which is not a controlled substance. It has a similar side-effect profile to stimulant medications but may, in addition, cause urinary hesitation or retention. The rate of response to atomoxetine may be slightly lower than that usually reported for stimulants (60% to 70% versus 70% to 80%) and it takes longer to work. Since this medication was only released in 2003, there is limited marketing data regarding its degree of efficacy in comparison to stimulants and the actual frequency of adverse effects. Potential side effects in adults include dry mouth, insomnia, nausea, constipation, decreased appetite, dizziness, sexual dysfunction, and urinary hesitancy or retention.⁵⁴ An advantage of atomoxetine over stimulants is its lower abuse potential. Atomoxetine and other first-line medications for the treatment of adult ADHD are listed in Table 3.⁵⁵⁻⁵⁷

Second-Line Medication Choices: Medications Not FDA-Approved for the Treatment of ADHD

Antidepressants. Antidepressants, including noradrenergic tricyclics (ie, nortriptyline and desipramine,^{47,58} venlafaxine [a dual norepinephrine serotonin reuptake inhibitor],⁵⁹ and bupropion [an indirect dopamine and norepinephrine agonist]⁴⁷) have suggested efficacy in treating ADHD in both adults and children who have comorbid depression.¹³ Antidepressant medications are regarded as less effective than stimulants in treating core ADHD symptoms.^{49,57,60} They are sometimes prescribed “off-label,” even to patients who are not depressed, because of their lower abuse potential

and their ability to treat concomitant depression, thus ameliorating those cognitive deficits due to depression symptomatology. The side-effect profiles of antidepressants have been well described and are generally well known by PCPs. Dosage guidelines for antidepressant medications in ADHD are generally similar to dosing guidelines for the treatment of depression.

Clonidine and Guanfacine. Clonidine and guanfacine are centrally acting α -adrenergic agonists which have been used to treat ADHD, although they are not FDA-approved for this use. They

are considered less effective than psychostimulants but may have utility as second-line treatments. Serious adverse events have been reported following the use of MPH in combination with clonidine, and the safety of this combination has not been systematically evaluated.⁵⁷

Pemoline. Pemoline is a dopamine and norepinephrine transporter inhibitor which has been used to treat ADHD for many years. Although it is FDA-approved for this use, it is considered a second-line treatment choice because of its association, in rare instances, with life-threatening hepatic failure.

Special Considerations and Risks of Medicating Adults for ADHD

Major Depression. The presence of certain comorbid psychiatric disorders may require modification of the pharmacologic treatment of ADHD. If a patient is depressed, treating the depression itself may improve ADHD symptoms, such as inattention and irritability, which makes it reasonable to treat the depression first. The PCP might choose, where appropriate, to treat the depression with bupropion, venlafaxine, or a tricyclic antidepressant, as these can be expected to ameliorate ADHD symp-

Table 3
First-Line Medication Choices Available for the Treatment of ADHD⁵⁵⁻⁵⁷

Form	Generic Medication	Brand-Name Medication	Starting Dose	Titration Rate and Typical Daily Dose	Duration of Action (in hours)	Daily Frequency
IR Stimulant Medications	Methylphenidate	Metadate, Methylin, Ritalin, others	5 mg BID	Increase by 10 mg/week to 0.5–1.0 mg/kg or 40–60 mg (80 mg maximum)	2–4	2–3
	Dexmethylphenidate	Focalin	2.5 mg BID	Increase by 2.5–5.0 mg BID weekly to 20 mg/day maximum	3–5	3–4
	D-amphetamine	Dexedrine, Dextrostat	5 mg/day	Increase by 5 mg QD over 3–7 days to 40 mg/day maximum	3–6	2–3
	D,L-amphetamine	Adderall	5 mg/day	Increase by 5 mg/week to 40 mg/day in divided doses	3–6	2–3
ER Stimulant Medications*	Methylphenidate	Metadate ER, Methylin ER, Ritalin SR	Metadate ER 10–20 mg/day; Ritalin SR 20 mg/day	Corresponds to 8 hour total dosage of IR tabs (maximum=60 mg)	4–8	2
	D-amphetamine	Dexedrine Spansule	5 mg/day	Increase by 5 mg QD over 3–7 days to 40 mg/day maximum	6–8	2
	Methylphenidate	Metadate CD, Ritalin LA	20 mg/day	Increase at intervals of ≥ 7 days until 1–2 mg/kg/day (60 mg/day maximum)	8–10 (bimodal peaks)	1–2
	Methylphenidate	Concerta	18 mg/day	Increase by 18 mg/week to 1–2 mg/kg/day or 54 mg maximum	8–12 (bimodal, ascending peaks)	1–2
	D,L-amphetamine	Adderall XR	5–10 mg/day	Increase by 5–10 mg/week to 30 mg/day maximum	10–12 (bimodal peaks)	1
ER Nonstimulant Medications	Atomoxetine	Strattera	40 mg/day	Increase by 40 mg every 3–7 days to a target of 80 mg/day or a maximum of 100 mg or 1.4 mg/kg	~24 (half-life= 5 hours)	1

* Titration with IR suggested first.

ADHD=attention-deficit/hyperactivity disorder; IR=immediate release; ER=extended release; SR=sustained release; CD=continuous delivery; LA=long acting; XR=extended release.

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toms to some extent. The PCP can then decide which ADHD symptoms remain and whether further treatment of the ADHD symptoms is indicated.

Bipolar Disorder. A significant minority of patients with depression may have undiagnosed bipolar disorder spectrum conditions. As there is some clinical overlap between ADHD symptoms and bipolar disorder, all depressed patients being evaluated for ADHD should be screened for bipolar disorder. It is important to directly question patients and family members about periods of elevated mood or energy as these are rarely spontaneously reported. The presence of any of the following should heighten a clinician's suspicions that bipolar disorder is a possibility: family history of bipolar disorder, depressive episodes characterized by hypersomnolence or "leaden paralysis," a history of abrupt switching out of depression after a few days on a low dose of an antidepressant, and/or a history of irritability or insomnia that persists even on very sedating antidepressants or sleep medications.

Extreme caution is urged in medicating patients with comorbid bipolar disorder. Clinicians should be alert for the emergence of hypomania or mania in patients who have a history of depression and are being treated for ADHD. Even at low doses, antidepressants and stimulants can precipitate manic episodes, accelerate mood cycling, or evoke psychotic symptoms, such as delusions or hallucinations. Atomoxetine would be expected to also carry a risk of mood destabilization in bipolar disorder. Until systematic clinical research establishes whether mood destabilization represents a significant risk in this situation, extreme caution is recommended.

The sleep deprivation resulting from medication side effects may also trigger mania in bipolar patients. Some stable medicated bipolar patients may tolerate stimulant therapy, but others may be destabilized even if they are concurrently on a mood stabilizer. Referral to a psychiatrist should be seriously considered for patients with known or strongly suspected bipolar disorder.

Aggression. Although stimulants can help reduce the impulsive aggression that is sometimes a feature of ADHD, there are forms of anger that go beyond flash temper or the quick irritability or outbursts seen in adult ADHD. Caution

should be exercised in using stimulants for patients with a history of rageful violence or explosive outbursts, since stimulants can increase rage reactions. In this context, it is prudent to conduct a careful safety assessment, including inquiry into access to any weapons. Psychiatric consultation is recommended in this instance.

Substance Abuse and Dependence. In the presence of significant substance abuse, the clinician should carefully monitor the patient's use of medications from other PCPs, as well as illicit drug abuse. In such cases, the clinician might consider selecting a nonaddictive medication, such as atomoxetine or one of the antidepressants. If stimulants must be used, the risks of exacerbating drug abuse may be tempered by having responsible family members control access to medication and have periodic visits with a family member to assess adherence to the treatment regimen. If a patient has a history of stimulant dependence, it may be prudent to recommend substance abuse treatment concurrently or before treatment for ADHD. If a patient has a history of misusing stimulants to self-medicate ADHD symptoms, then limiting prescriptions to small quantities can be considered.

Anxiety Disorders. Although stimulants have been reported to reduce anxiety in many adults with ADHD and comorbid generalized anxiety disorder,¹⁸ stimulants may also exacerbate anxiety in patients with comorbid ADHD and anxiety disorders. In such cases, treating the anxiety disorder along with the ADHD may pose a therapeutic challenge that bears close clinical monitoring. Use of antidepressants or nonstimulant medications, as well as adjunctive psychotherapy, should be considered.

Comorbid Medical Conditions. A variety of other medical conditions, from pregnancy to comorbid cardiac disease, require special consideration and possibly consultation with or referral to a specialist. Both stimulants and atomoxetine need to be used with caution in patients with hypertension, cardiovascular or cerebrovascular disease, and supraventricular tachycardia. Atomoxetine is not recommended in patients with narrow-angle glaucoma, and doses should be adjusted in patients with hepatic dysfunction.

Finally, there are some adults with

ADHD and comorbid medical disorders for whom the risks of treatment with currently available medications may outweigh the potential benefits, and the clinician may decide against prescribing.

Psychological Treatment Options

Nonpharmacologic interventions include education about ADHD, and psychotherapy. Adults with ADHD need to be educated about their disorder in order to learn what they can do to make their lives easier and more productive. Psychoeducation can be validating and therapeutic to adults who have struggled for years with their symptoms and have attributed poor achievement to personal failings. Psychotherapy can help patients to understand how their behaviors affect themselves and others and may help to motivate them to seek more adaptive ways of managing their environment and activities. Training in life management skills and organizational techniques may be helpful as well.

Some patients with adult ADHD can be helped by ADHD coaching. The role of the coach includes assessing how ADHD impairs a particular patient's functioning, providing psychoeducation, and helping implement remediation strategies aimed at restructuring the patient's environment, to minimize the effect of ADHD symptoms on organization and efficiency. For example, ADHD coaches can guide patients in manipulating their environments to set up work centers that minimize visual and auditory distractions. The coach may recommend organizational strategies, such as using beepers or making daily lists. Finally, the coach can also be an influential cheerleader, encouraging and supporting the patient to implement and sustain useful changes in behavior.

Environmental Interventions

Given the difficulties that patients with ADHD encounter, environmental distractions can be a major problem. An environment relatively free of distractions and with appropriate structure can provide significant help. Environmental engineering may benefit adults with ADHD. For example, adults with ADHD may benefit from quiet work areas and work schedules seeded with strategic breaks. Job counseling may be of significant value since the limitations imposed by ADHD

symptoms can be far less detrimental in some vocational settings than in others. For those patients whose responsibilities and finances support it, a secretary or executive assistant can handle aspects of the work which the patient finds difficult. Similarly, the patient and family members can help structure a home life which maximizes the patient's strengths and avoids many pitfalls associated with the patient's vulnerabilities. However, the stress of these demands on spouses and family members should not be ignored. Involvement of the family and significant others in psychoeducation and psychotherapy can be vital to the long-term success of treatment.

Since adult ADHD is a chronic disorder, many will need treatment indefinitely, and those placed on medications for ADHD need to be assessed longitudinally. The clinician and patient should jointly identify specific target symptoms, behaviors, and goals to be monitored over time so that decisions can be made about whether to continue active treatment. In the early stages of treatment, the clinician should assess the degree of response and side effects to medication, and adjust types and dosages of medications. Frequent follow-up appointments from a few weeks to a month apart should be scheduled. In later stages of treatment, less frequent visits may be needed. Once maximal clinical benefit has been achieved, the clinician should discuss issues such as drug holidays, frequency of medication dosing throughout the day, and medication-free weekends. The range of long-term outcomes of treating adult ADHD has yet to be determined, but what is known so far speaks to the need for active intervention and thoughtful long-term follow-up.

Conclusion

Adult ADHD is a neurobiologic disorder that is prevalent and under-recognized, is challenging to diagnose, has symptoms that are not just the result of lifestyle choices or moral weakness, and is treatment responsive. As more practical and effective treatments become available, the public is becoming more aware of the existence of ADHD throughout the life cycle and adults are more frequently presenting for diagnosis and treatment. If left

untreated, ADHD can cause significant impairment throughout the life cycle. Diagnosis can lead to far-reaching changes. Psychoeducation can help affected individuals to understand why their biology and environment may be conspiring to thwart their ability to achieve their full potential. Treatment of ADHD can improve social and occupational functioning and self-esteem and reduce impulsive high-risk behaviors. With diagnosis and treatment, many adults whose early promise and good intentions have yielded to overwhelming personal and professional struggles can gain new self-perspective and hope. Several books for clinicians,⁶⁰⁻⁶⁴ books for patients,⁶⁵⁻⁶⁷ and Web sites⁶⁸⁻⁷¹ may provide more guidance on this topic. **PP**

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