Management of ADHD in Adults

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Although first identified in children in the 19th century, attention-deficit/hyperactivity disorder (ADHD) in adults was not described in the literature until 1976. The symptoms of adult ADHD resemble the symptoms of childhood ADHD, but symptom intensity, especially hyperactivity, may decrease over time. However, due to the challenges and responsibilities of adulthood, a normal day is extremely complicated for the ADHD adult. Molecular genetics and neuroimaging studies confirm that ADHD is a heterogeneous, neurobiological disorder, mainly of dopaminergic and noradrenergic pathways. Trials of pharmacologic treatments in adults with ADHD have produced mixed results due to considerable variability in diagnostic criteria, dosing, and response. This article reviews the history, neurobiology, and pharmacologic management of adult ADHD.

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HISTORY OF ADULT ADHD

Attention-deficit/hyperactivity disorder (ADHD) is characterized by inattentiveness, overactivity, and impulsiveness. Although ADHD was first identified in children in the 19th century, adult ADHD was not described in the literature until 1976, when Wood et al.[1] showed evidence of response to stimulants in a group of adults who presented with the same symptoms as ADHD children.

Encephalitis lethargica, also called von Economo's disease, has been used as a model of ADHD. After the post–World War I pandemic of encephalitis lethargica (1916–1927), some children and adolescents had a postencephalitic behavioral syndrome characterized by overactivity, lack of coordination, learning disability, impulsivity, and aggression.[2,3] The children were reported as having minimal brain dysfunction–like behavior, and the adults exhibited parkinsonian symptoms. The patients became severely rigid with tremor, they had pathologic restlessness and akathisia, and they developed formal basal ganglia lesions. The basal ganglia lesions were the first clue that states of pathologic restlessness are not driven purely dynamically or in terms of conflict. This discovery represents a dividing point in the neurologic and the neuropsychiatric perspectives on syndromes of pathologic restlessness. Subsequent studies have implicated frontal lobe dysfunction in the pathophysiology of ADHD.[4] Von Economo described formerly normal children becoming more talkative, importunate, impertinent, forward, and disrespectful. Although his observations described children predominantly with a conduct disorder, he also noted an incapacity for sustained attention.[2]

EVOLUTION OF DIAGNOSTIC CRITERIA

In 1980, the third edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III)[5] was published with 2 major changes in emphasis and terminology for what had been previously referred to as *hyperkinetic syndrome* (Table 1).[2] Attempts to include etiology within the definition and diagnostic terminology were abandoned in favor of a phenomenological approach using operational criteria. Another change involved the consensus that inattentiveness was a central criterion and that impulsiveness was as important as overactivity. Therefore, DSM-III used the classification attention-deficit disorder, which could be diagnosed with or without hyperactivity (ADD-H or ADD). Experts also agreed that the disorder often persisted into adulthood but remained vague about the adult symptoms. The later revision of DSM-III, DSM-III-R,[6] allowed formal classification into adulthood and required the symptom onset in childhood, but it also returned to placing more emphasis on overactivity, hence the change from ADD to ADHD. With the publication of the fourth edition of DSM (DSM-IV)[7] in 1994, there remained a distinction between inattention and the other symptom clusters, but impulsive and hyperactive symptoms remained in the same list, although separately identified.[2] The traits described by von Economo in his observations of postencephalitic children still remain the criteria for diagnosis of ADHD in DSM-IV.

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Table 1. Evolving Diagnostic Criteria for ADHD[a]

DSM-III	Name changed from hyperkinetic syndrome to attention deficit disorder
	Phenomenological approach
	Inattentiveness central to diagnosis
	More emphasis on impulsiveness
	Can be diagnosed without hyperactivity
DSM-III-R	Formal classification into adulthood
	Required symptom onset in childhood
	More emphasis on overactivity
	Name changed to attention-deficit/hyperactivity disorder
DSM-IV	Impulsive and hyperactive symptoms in same list but separately identified
	Distinction between inattention and other symptom clusters

[a]From Arnold and Jensen.[2]

ADULT VS. CHILDHOOD ADHD

In adults, the symptoms of ADHD are seen not in the school setting as with children but in the workplace. The symptoms also have to be present in one other setting, such as at home, according to DSM-IV criteria.[7] When comparing childhood with adult ADHD, the symptoms a patient has as a child are the symptoms the patient tends to have as an adult. Symptom intensity, especially hyperactivity, may decrease over time, and while there may be cases of unrecognized ADHD until adulthood, adult onset is not thought to occur. Despite a decrease in ADHD symptom intensity in adulthood, everyday life continues to become more complex. Adults without ADHD have a very full, challenging day, but an adult with ADHD is particularly challenged by a normal day's activities. Not only do adults with ADHD have to get themselves up and functioning in the morning, make it to work on time, and be productive, but they also have to get their children, who many times have ADHD themselves, out of bed and functioning in the morning and off to school. After a full day of work, ADHD adults must manage homework and dinner, get the children to bed, and somehow try to find some time for themselves. With all the problems these patients have with executive functioning and time management, what seems like a very normal day to the average individual is an extremely complicated task for the adult with ADHD. For this reason, clinicians who treat adults with ADHD must examine whole-life issues.

ETIOLOGY OF ADHD

In determining the validity of adult ADHD as a diagnosis, many clinical correlates must be considered. Faraone et al.[8] reviewed clinical, family, psychopharmacologic, neurobiological, and outcome studies. They found that family history, treatment response, course and outcome, molecular genetics, and neuroimaging combine to tell a very interesting story. The reports described adults with clinical features highly reminiscent of childhood ADHD. Many of the adults with ADHD suffered from comorbid psychiatric disorders and showed clinically significant impairments, such as histories of school failure, occupational problems, and traffic accidents. Family history is important in diagnosis because there is a strong genetic component with about a 50% concordance rate for ADHD in first-degree relatives.[9,10]

MOLECULAR GENETICS AND NEUROIMAGING

Data from molecular genetics and neuroimaging studies also support the validity of ADHD in adults. Several studies have reported that ADHD is a heterogeneous disorder[11,12] that has been associated with the 10-repeat allele of the 40 bp at the dopamine transporter gene (*DAT1*)[13–16] and the 7-repeat allele of the 48 bp in exon III of the dopamine D_4 receptor gene (*DRD4*).[13,14,17–19]

That ADHD is a neurobiological disorder, mainly of dopaminergic and noradrenergic pathways, is supported by evidence from single-photon emission computed tomography/positron emission tomography (SPECT/PET) studies[20–23] and magnetic resonance imaging (MRI) studies.[24–26] Ernst et al.[21] used PET with [fluorine-18] fluorodopa ([^{18}F] FDOPA) to assess the integrity of dopaminergic presynaptic function in ADHD. Data obtained through this process reflect DOPA decarboxylase activity and dopamine storage processes. They found that adults with ADHD have abnormally low DOPA decarboxylase activity in the prefrontal cortex, particularly in the medial and left lateral areas. By using PET with [^{18}F] fluoro-2-deoxy-D-glucose, Zametkin et al.[22] were able to measure the regional glucose metabolism in the brains of adults with ADHD. Their results confirmed previous imaging study findings of abnormal regional and global glucose metabolism in the brains of adults with ADHD since childhood. The largest areas of reduction in glucose metabolism were the premotor cortex and the superior prefrontal cortex—areas earlier shown to be involved in the control of attention and motor activity. Impaired executive function has been associated with damage in the frontal lobes,[2] and excessive motor activity has been associated with damage in the basal ganglia.[27]

PHARMACOLOGIC TREATMENT OF ADHD

Although educational therapy and psychotherapy are often beneficial for developing skills to cope with the challenges of ADHD, pharmacologic treatment is the mainstay of treatment for children and adults with ADHD. The MTA Cooperative Group study[28] of long-term (14-month) treatments for children with ADHD found significant improvement with stimulant medication treatment, with or without psychosocial treatments compared with intensive behavioral treatment and/or community care alone. Far more medication trials have been conducted with children and

Table 2. Stimulant Trials in Adult ADHD[a]

Study	Diagnostic Criteria	N	Design	Drug	Duration (wk)	Response Rate
Methylphenidate						
Wood et al[1]	RDC	11	Double-blind placebo-controlled crossover	Methylphenidate	4	+
		15	Open-label	Pemoline or tricyclic		+
Mattes et al[32]	DSM-III	61	Double-blind placebo-controlled crossover	Methylphenidate	6	–
Wender et al[33]	DSM-III	37	Double-blind placebo-controlled crossover	Methylphenidate	5	+
Gualtieri et al[34]	DSM-III	22	Double-blind placebo-controlled crossover	Methylphenidate	2	+/–
Spencer et al[35]	DSM-III-R	23	Double-blind placebo-controlled crossover	Methylphenidate	7	+
Shekim et al[36]	DSM-III-R	33	Open-label	Methylphenidate	8	–
Pemoline and mixed amphetamines						
Spencer et al[37]	DSM-IV	27	Double-blind placebo-controlled crossover	Mixed amphetamines	7	+
Horrigan and Barnhill[38]	DSM-III	24	Open-label	Mixed amphetamines	16	+
Wilens et al[39]	DSM-IV	42	Double-blind placebo-controlled crossover	Pemoline	10	+
Wilens et al[40]	DSM-III-R and DSM-IV	27	Double-blind placebo-controlled crossover	Pemoline	10	–

[a]Abbreviations: ADHD = attention-deficit/hyperactivity disorder, RDC = Research Diagnostic Criteria of Spitzer et al.[31] Symbols: + = ≥ 50% of all patients taking study medication showed a positive response, – = < 50% of all patients taking study medication showed a positive response, +/– = mixed results.

adolescents than with adults; however, similar medications are used for both children and adults with ADHD. Wilens et al.[29] reviewed comprehensively the available literature on pharmacologic treatment of adult ADHD in 2002. Stimulants such as methylphenidate, pemoline, or amphetamine preparations or antidepressants such as norepinephrine reuptake inhibitors, norepinephrine-serotonin reuptake inhibitors, or norepinephrine-dopamine reuptake inhibitors make up the most widely used treatments for ADHD. Data from those studies, in addition to the results of subsequent trials, are bringing clinicians closer to understanding and effectively treating adults suffering from ADHD.

Stimulant Trials

A review of 11 stimulant trials conducted between 1976 and 2001 in adults (N = 300) with ADHD shows response rates that are less consistent than the response rates in similar trials with children (Table 2).[30] The results of the earlier studies were inconsistent, which could be the result of using lower stimulant doses and less stringent inclusion criteria than were used in later trials.

Methylphenidate. In one of the earliest trials of pharmacologic treatment of ADHD in adults, Wood et al.[1] conducted a double-blind trial of methylphenidate in 11 of 15 patients, and an open trial of pemoline, imipramine, or amitriptyline in all 15 patients. Patients were diagnosed with minimal brain dysfunction according to the Research Diagnostic Criteria of Spitzer et al.[31] Eight of the 11 patients taking methylphenidate showed a significant response to the double-blind trial of methylphenidate. Of all 15 patients participating in the open trial of pemoline, imipramine, or amitriptyline, 8 showed a good response to stimulants or tricyclic antidepressants, 2 showed a moderately favorable response, and 5 were unresponsive to drug therapy. In another double-blind crossover trial[32] with methylphenidate and placebo, 26 of the 61 completers had a childhood diagnosis of ADD-H according to DSM-III criteria, and 35 comparators had similar adult symptoms but no history of childhood ADD-H. At endpoint, only 25% of the patients were considered responders.

Wender et al.[33] had more favorable results for methylphenidate. The mean dose of methylphenidate after 14 days was 43.2 mg/day. Of the 37 completers, 21 (57%) experienced a moderate-to-marked treatment response during the methylphenidate condition, 12 (32%) demonstrated little or no change during either treatment condition, and 4 (11%) demonstrated a moderate-to-marked response to placebo and either no benefit or mild worsening with methylphenidate. In a study of methylphenidate conducted by Gualtieri et al.,[34] 8 patients showed a mild-to-moderate response after 2 weeks of treatment, while Iaboni, using a similar study design, but over 4 weeks, showed moderate improvement in 30 patients (as reviewed in Wilens et al.[29]). Another double-blind, placebo-controlled study by Spencer et al.[35] found a marked therapeutic response in 18 (78%) of 23 patients while taking methylphenidate, compared with 1 patient (4%) while taking placebo. In this study, 23 adult patients were treated with relatively high doses of 1 mg/kg/day. In an open-label study by Shekim et al.,[36] methylphenidate produced a favorable response in 78% of the 33 patients enrolled.

Pemoline and mixed amphetamine salts. Other clinical trials on pharmacologic treatments for adult ADHD have focused on the use of pemoline and mixed amphetamine salts. In a trial of mixed amphetamine salts, Spencer et al.[37] examined 27 adults satisfying full DSM-IV criteria for ADHD. The 7-week, randomized, double-blind, placebo-controlled, crossover study used approximately 54 mg/day of mixed amphetamine. Of the 27 patients taking mixed amphetamine, 19 (70%) showed improvement

Table 3. Nonstimulant Trials in Adult ADHD[a]

Study	Diagnostic Criteria	N	Design	Drug	Duration (wk)	Response Rate
Antidepressants: norepinephrine, dopamine, serotonin reuptake inhibitors						
Wilens et al[42]	DSM-III-R	37	Retrospective chart review	Desipramine, nortriptyline	50	+
Wilens et al[43]	DSM-IV	43	Double-blind parallel	Desipramine	6	+
Wender and Reimherr[44]	WURS	14	Open-label	Bupropion	14	+
Wilens et al[45]	DSM-IV	38	Double-blind placebo-controlled parallel	Bupropion SR	6	+
Findling et al[46]	DSM-IV	9	Open-label	Venlafaxine	8	+
Wilens et al[47]	DSM-IV	2	Open-label case reports	Venlafaxine	…	+
Adler et al[48]	DSM-III-R	12	Open-label	Venlafaxine	8	+
Hedges et al[49]	DSM-III-R	11	Open-label	Venlafaxine	8	+
Specific norepinephrine reuptake inhibitors						
Spencer et al[50]	DSM-III-R	21	Double-blind crossover	Atomoxetine	7	+/–
Michelson et al[51]	DSM-IV	536	Double-blind placebo-controlled	Atomoxetine	10	+
Antihypertensives						
Mattes[52]	DSM-III	13	Open retrospective	Propranolol	3–50	+
Taylor and Russo[53]	DSM-IV	17	Double-blind placebo-controlled crossover	Guanfacine	7	+
Amino acids						
Reimherr et al[54]	DSM-III	12	Open-label	L-tyrosine	8	–
Cholinergic agents and nicotine						
Conners et al[55]	DSM-IV	11	Double-blind placebo-controlled crossover	Nicotine patch	2 days	+
Wilens et al[56]	DSM-IV	29	Double-blind placebo-controlled crossover	ABT-418	7	+/–
Antinarcoleptic medication						
Taylor[57]	DSM-IV	21	Double-blind crossover	Modafinil vs amphetamines	7	+
Modafinil press release[58]	DSM-IV	113	Double-blind placebo-controlled crossover	Modafinil	7	–

[a]Abbreviations: ADHD = attention-deficit/hyperactivity disorder, SR = sustained-release, WURS = Wender Utah Rating Scale. Symbols: + = ≥ 50% of all patients taking study medication showed a positive response, – = < 50% of all patients taking study medication showed a positive response, +/– = mixed results, … = unknown.

of ADHD symptoms, compared with 2 (7%) of 27 patients taking placebo. In an open-label 16-week trial using dextroamphetamine/amphetamine, Horrigan and Barnhill[38] reported that of 24 adult patients with ADHD, as measured by the Clinical Global Impressions-Improvement (CGI-I) scale scores, 13 (54%) were considered responders. The mean end-dose of the responders was 10.77 mg/day, and the study also reported acute anxiety symptoms in 4 of 7 patients with comorbid anxiety disorders.

The use of pemoline for the treatment of adult ADHD was studied in 2 trials. Wilens et al.,[39] reported positive response rates in 42 patients treated in a double-blind placebo-controlled study. A later study[40] utilized the same design with 35 patients diagnosed with DSM-IV ADHD, but higher mean doses of 2.2 mg/kg/day resulted in only a moderate (50%) response rate, defined by a 30% reduction of ADHD symptoms. The modest clinical utility of pemoline is overshadowed by the association of this agent with liver toxicity.[40,41]

The studies reviewed in this section demonstrate the efficacy of stimulants in adults with ADHD. In general, efficacy was somewhat greater in the later studies, which used more consistent diagnostic criteria and higher doses of the stimulants being studied.

Nonstimulant Trials

Trials of nonstimulants in adults include a variety of agents with dopaminergic and/or noradrenergic action (Table 3). Many of the agents described below have been studied in relation to the treatment of ADHD in children, and again, the results of clinical trials of these nonstimulant medications on adult patients with ADHD are generally reflective of findings in the pediatric studies.

Antidepressants. Antidepressants have been used as alternative pharmacologic agents for the treatment of ADHD in children, and various classes of antidepressants, including the tricyclics, monoamine oxidase inhibitors, and selective serotonin reuptake inhibitors, have produced variable results in the patients studied.

The earliest group of antidepressants studied for use in the treatment of ADHD in adults were the tricyclics. A 1995 chart review by Wilens et al.[42] suggested that desipramine, which is mostly noradrenergic in its mechanism of action, and nortriptyline, a norepinephrine and serotonin reuptake inhibitor, used in combination with stimulants and other psychotropics were able to moderately improve the symptoms of the 37 adult ADHD patients reviewed. A double-blind, parallel trial of desipramine[43] in 43 patients showed moderate responses, but only at higher doses.

Wender and Reimherr[44] conducted an open-label trial of bupropion, an atypical catecholaminergic (dopamine and norepinephrine) antidepressant, in 14 adults with ADHD. The patients had received maintenance stimulant medication or monoamine oxidase inhibitors for an average of 3.7 years. The mean ± SD dose of bupropion was 359 ± 118 mg/day (range, 150–450 mg/day). After 6 to 8 weeks of bupropion treatment, 8 of the 14 patients were considered very much improved, 6 were considered much improved,

and 10 chose to continue bupropion treatment. Wilens et al.[45] conducted a double-blind, placebo-controlled, randomized, parallel, 6-week trial comparing sustained-release bupropion (up to 200 mg b.i.d.) with placebo. The 38 patients who completed the study met DSM-IV criteria for ADHD, and 16 (76%) of the patients taking bupropion responded positively versus 7 (37%) of the patients taking placebo.

In trials of other antidepressant agents, there have been small, open-label studies in adults with venlafaxine, an antidepressant with both serotonergic and noradrenergic properties. In these trials, patients reported better tolerance with venlafaxine than with other drugs. Findling et al.[46] studied 10 adult patients who met DSM-IV criteria for ADHD in an 8-week open trial of venlafaxine. Patients were started on an initial dose of 37.5 mg b.i.d., which was increased to 75 mg b.i.d. as needed. On the basis of a priori criteria, 7 of the 9 completers were considered responders. Wilens et al.[47] reported on 2 cases of adult ADHD that were successfully treated with venlafaxine after failure with stimulants and antidepressants among other medications. Two other clinical trials of venlafaxine[48,49] reported significant reductions in ADHD symptoms, although 38% of patients enrolled in the 2 studies were unable to tolerate the relatively high doses of venlafaxine used.

Specific norepinephrine reuptake inhibitors. Atomoxetine is a nonstimulant, selective norepinephrine reuptake inhibitor that is currently being investigated for the treatment of ADHD in children, adolescents, and adults.[59] It is currently under review by the U.S. Food and Drug Administration (FDA) for the treatment of both children and adults with ADHD.

The original examination of atomoxetine for ADHD was in a trial by Spencer and colleagues[50] in 1998. They conducted a double-blind, placebo-controlled, crossover trial of atomoxetine in 22 adults who met DSM-III-R criteria for ADHD. Of the 22 patients, 1 patient dropped out due to adverse effects. The mean dose of atomoxetine at week 3 was 76 mg/day. Using a preestablished definition of improvement of ≥ 30% reduction in symptoms, they found that 11 of 21 patients showed improvement in ADHD symptoms while receiving atomoxetine, compared with 2 who improved while receiving placebo.

A trial consisting of 2 parallel, identical studies was recently completed by Michelson et al.[51] in 536 adult patients with ADHD. The primary objective of the study was to examine the efficacy of atomoxetine at doses of 60 to 120 mg/day in 2 equally divided doses compared with placebo for up to 10 weeks. The study design consisted of an initial screening with a washout and entry period and 2 weeks of placebo lead-in followed by 10 weeks of acute active treatment. The initial active treatment dose was 30 mg/day b.i.d. and titrated to a maximum dose of 60 mg/day b.i.d. An interesting aspect of the study is that it used blinded rating investigators and non-blinded treating physicians, which adds a further measure of control. Entry into the study required meeting DSM-IV ADHD criteria and either having corroborated childhood symptoms by report of the patient or having current symptoms reported by a significant other.

Potential advantages of atomoxetine, compared with stimulants, include a longer duration of action, a lower risk of rebound, and a lower risk of induction of tics or psychosis. If the FDA does not require scheduling for atomoxetine, additional advantages over stimulants would be the ease of prescribing and lower abuse liability in patients with ADHD and comorbid substance abuse disorders.

Antihypertensive agents. The use of antihypertensive pharmacologic agents in adult patients with ADHD has focused on the ability of these agents to reduce the aggressiveness, temper outbursts, and marked hyperactivity features of ADHD. In an open study of propranolol,[52] 13 adults with a DSM-III diagnosis of residual ADD were given a maximum dose of 160 mg/day. Of the 13 patients, 11 demonstrated improvement in symptoms of ADD.

Taylor and Russo[53] conducted a double-blind, crossover, 7-week trial of guanfacine, an α-adrenergic agonist, in 17 adults with ADHD. The results showed that guanfacine was well-tolerated and improved the neuropsychiatric functioning of all 17 patients, as compared with placebo treatment.

Amino acids. The use of the amino acids L-dopa and L-tyrosine for the treatment of adult ADHD in the 1980s was based on the theory that the symptoms of ADHD could be related to deficiencies in the catecholaminergic system. Reimherr et al.[54] conducted an 8-week open trial of L-tyrosine in 12 patients with ADD, residual type, according to DSM-III diagnostic criteria. The dose of L-tyrosine was rapidly titrated from 50 mg/kg/day to 150 mg/kg/day with only minor side effects. In the initial phase, patients appeared to stabilize at 4 weeks, at which time there was marked improvement in 2 patients, moderate improvement in 6, slight or no improvement in 2, and slight worsening in 2. Although there remained significant effects from baseline to week 8, clinical regression occurred between the subjects' best responses and their responses at 8 weeks.

Cholinergic agents and nicotine. The observation that cigarette smoking appeared to have a pathoplastic effect on the adult ADHD population led to a short 2-day trial of a nicotine patch in 11 patients.[55] All patients demonstrated significantly reduced ADHD symptoms and improved cognition.

The Abbott Laboratories (Abbott Park, Ill.) compound ABT-418 is a novel cholinergic agonist (nicotinic analog). A double-blind, placebo-controlled, randomized, crossover trial was conducted by Wilens et al.[56] that compared a 75-mg transdermal patch of ABT-418 with a placebo patch in adults who met DSM-IV criteria for ADHD. The 29 completers participated in a 3-week treatment period,

followed by 1 week of washout and an additional 3-week treatment period. At the endpoint of each active arm (last observation carried forward), 40% of patients taking ABT-418 were considered improved, compared with 13% of patients taking placebo. Similarly, at endpoint there was a significantly greater reduction in ADHD symptom checklist scores (28% vs. 15%).

Antinarcoleptic/alertness medications. Among the newer agents used to treat ADHD, the alertness-enhancing antinarcoleptic medications have been shown to have limited efficacy in the reduction of ADHD symptoms. Taylor[57] studied modafinil in a double-blind, crossover study with amphetamines (N = 22) and found that both agents appeared to be equally effective, producing a 48% response rate in both groups. In a larger, industry-sponsored study[58] of the same agent, with 113 subjects, the response rates obtained by Taylor with modafinil could not be replicated.

SUMMARY

Although identified much later than childhood ADHD, adult ADHD is a valid, common, and impairing neuropsychiatric condition occurring in up to 4% of adults.[60] Adults and children with ADHD share a similar core symptom presentation, including inattention, distractibility, forgetfulness, and impulsiveness. Hyperactivity tends to decrease in intensity over time and often presents as a sense of internal restlessness in adults. However, adults have more complex lives, with more cognitively demanding tasks and longer days than children. Therefore, although stimulant medications have been shown to be effective treatments for adults with ADHD, the unique, whole-life needs of the adult population require medications with a longer duration of action. Longer-acting preparations of stimulant medications, such as methylphenidate and mixed amphetamine salts, have made great strides toward meeting this need. However, a preliminary survey[61] of preadolescent, adolescent, and adult patients treated in an ADHD program found that 39% of patients treated with a longer-acting methylphenidate preparation required additional treatment with a short-acting stimulant either to amplify the therapeutic effects in the morning or to extend the therapeutic duration later in the day. Further development of nonstimulant treatments for ADHD is likely to provide a substantial therapeutic alternative for adults with this condition.

Drug names: amitriptyline (Elavil, Endep, and others), bupropion (Wellbutrin and others), desipramine (Norpramin and others), dextroamphetamine/amphetamine (Adderall), guanfacine (Tenex and others), imipramine (Tofranil, Surmontil, and others), methylphenidate (Focalin, Metadate CD, and others), modafinil (Provigil), nortriptyline (Aventyl, Pamelor, and others), pemoline (Cylert and others), propranolol (Inderal and others), venlafaxine (Effexor).

Disclosure of off-label usage: The authors of this article have determined that, to the best of their knowledge, amitriptyline, bupropion, desipramine, guanfacine, imipramine, modafinil, nortriptyline, propranolol, venlafaxine, ABT-418, atomoxetine, L-dopa, and L-tyrosine are not approved by the U.S. Food and Drug Administration for the treatment of attention-deficit/hyperactivity disorder (ADHD); and dextroamphetamine/amphetamine, methylphenidate, and pemoline are not approved for the treatment of ADHD in adults.

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