

ADHD in Adults - A Guide for the Primary Care Physician

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## **Abstract and Introduction**

### **Abstract**

Attention deficit hyperactivity disorder (ADHD) persists into adulthood in up to 60% of cases with childhood onset. A childhood history of ADHD is a prerequisite for making the ADHD diagnosis in an adult. The Utah, Copeland, and Brown self-rating scales are useful in helping the primary care physician confirm the diagnosis. A thorough developmental history, a substance abuse history, and a medical and neurologic examination should be obtained to rule out other causes of poor concentration and attention. Medication interventions can include the stimulants and/or noradrenergic and dopaminergic antidepressants. Nonmedication intervention should include education, referral to support groups, and referral for individual and/or couples therapy. If the diagnosis is unclear or if there is inadequate response to an intervention, referral to a psychiatrist or psychologist is indicated.

### **Introduction**

The DSM-IV describes the core feature of attention deficit hyperactivity disorder (ADHD) as "a persistent pattern of inattention and/or hyperactivity-impulsivity that is more frequent and severe than is typically found in individuals at a comparable level of development."<sup>[1]</sup> As the name implies, patients with ADHD have symptoms related to an inability to regulate their attention and/or an inability to monitor their motor behavior or impulses.

Diagnosis and treatment of ADHD in children is common, but the same diagnosis in adults remains controversial. In 1994, Shaffer<sup>[2]</sup> noted several reasons for such skepticism. First, it is relatively difficult to get an accurate history to verify the requisite childhood onset of the symptoms. Second, the significant comorbidity with adult ADHD makes sorting out the diagnosis from other disorders difficult. Third, although there is a great deal of anecdotal evidence for treatment of adult ADHD with stimulant medication, there is a relative lack of literature documenting its effectiveness.<sup>[2]</sup> Also, as Spencer et al<sup>[3]</sup> pointed out, the fact that ADHD often is a self-diagnosed condition further complicates the skepticism. This skepticism

perhaps is increased in the primary care setting because the most common therapy for the self-diagnosed condition is a controlled drug.

Early research suggested that ADHD should resolve with age and maturation and that initial perception of ADHD as primarily a childhood disorder has been an obstacle for diagnosis and treatment in adults. However, follow-up studies have suggested that up to 60% of children with ADHD will have symptoms persisting into adulthood.<sup>[3]</sup> In their review of more than 1,700 cases of adults with ADHD diagnosed in childhood, Spencer et al<sup>[4]</sup> found that 663 of those studied continued to meet criteria for ADHD as adults. Borland and Heckman<sup>[5]</sup> compared adults who had ADHD with their normal siblings. They found that 50% of the adults with ADHD diagnosed during childhood had a syndrome of restlessness, difficulty with concentration, and impulsive behavior that persisted into adulthood, as opposed to just 5% of their unaffected siblings. That ADHD indeed does persist into adulthood and the growing perception that the adult version carries with it a significant comorbidity with affective, anxiety, personality, and substance abuse disorders has brought about a growing recognition that addressing adult ADHD should be an area of investigation and treatment.

Accurate diagnosis and treatment of attention deficit disorder in the primary care setting requires an accurate and thorough developmental history, recognition of the core features of the disorder, and a working knowledge of the neurobiology, psychopharmacology, and behavioral treatment of ADHD.

## **Diagnosis**

The DSM-IV delineates between the hyperactive, the inattentive, and the combined hyperactive and inattentive subtypes of attention deficit disorder.<sup>1</sup> Diagnosis of ADHD in adults has as a prerequisite the presence of ADHD symptoms during childhood. Because the diagnosis of ADHD in adults often is difficult, the Utah Rating Scale was developed to aid in retroactive diagnosis of childhood ADHD. Essentially, the Utah criteria require a diagnosis in childhood by the narrow DSM-IV criteria for children, Connors' Parent Rating Scale results in the 95th percentile, or meeting broad criteria by history. The broad criteria for childhood diagnosis include hyperactivity, attention deficits, and at least one of the following: behavior problems in school, impulsivity, overexcitability, or temper outbursts. Adult criteria would include motor hyperactivity, attention deficits, affective lability, "hot temper," emotional overreactivity, disorganization and inability to complete tasks, impulsivity, and other "associated features."<sup>[6]</sup>

However, the Utah criteria tend to exclude patients who have a history of inattentiveness without hyperactivity. The inattentive subtype of ADHD can present itself in several ways. Inability to screen out irrelevant stimuli (distractibility), poor organizational skills, and inability to focus for extended periods on a specific task are all examples of the inattentive symptoms of ADHD. Also, inability to attend to details at work or school, forgetfulness, and repeated careless errors with details, paperwork, sequential types of tasks, or directions are characteristic of ADHD in adults. Because attention deficit disorder is a

disorder of attention regulation and prioritization, patients sometimes will report that they "hyper-focus" on relatively unimportant details to the exclusion of more important or more pressing issues.

Frequently, the overt hyperactive symptoms of childhood will resolve or at least change in adults. Common adult ADHD characteristics include stubbornness, chronic conflicts with authority, difficulty in spouse and peer relationships, frequent job changes, poor frustration tolerance, and poor academic performance despite adequate or even superior intellectual abilities. They frequently report feeling scattered and being chronically late for appointments, anxious, irritable, and overwhelmed with tasks of daily living. A common precipitant for an increase in depressive or anxiety symptoms is an increase in responsibility at home, work, or school.

Two self-rating scales, the Copeland Symptom Checklist for Adult ADHD and the Brown Adult ADD Scale, are useful for the primary care physician. The Copeland list consists of 63 questions assessing a broad range of cognitive and emotional symptoms as well as an assessment of the emotional impact of those symptoms.<sup>[7]</sup> The Brown scale consists of 40 questions assessing the cognitive symptoms associated with difficulty initiating and maintaining optimal concentration and arousal level.<sup>[8]</sup>

Adult patients with ADHD often see primary care physicians reporting anxiety, depressive or affective symptoms, substance abuse, and/or conflicts at home, work, or school. Sorting out the diagnosis in the midst of significant comorbidity superimposed on many years of coping with the disorder can be difficult. If the diagnosis remains unclear after obtaining a history and administering a rating scale or if there is significant and confusing overlap with comorbid psychiatric disorders, a referral to a psychologist or psychiatrist is indicated.

## **Illustrative Cases**

### **Case 1**

This 39 year-old man had a history of diagnosed bipolar disorder. His family physician reported that the patient appeared "manic" during his last office visit. The patient described a lifelong history of being "hyperactive" and had a school history significant for underachievement (despite above-average intelligence), distractibility, fighting, and impulsive behavior. On interview, he was circumstantial, tangential, and talkative; he often interrupted the examiner and was difficult to interview in a structured manner. He described an adult history of impulsive spending, irritability, temper outbursts, and multiple job and relationship changes. Despite the diagnosis of bipolar disorder, he had never had a discrete manic episode distinct from his baseline behavior pattern. He did report that he became angry easily and had been fired from several jobs because of conflicts with authority figures. He also described himself as a poor money manager; however, he denied any history of spending sprees, hyperreligiosity, grandiosity, hypersexual behavior, or other symptoms of mania.

He had been treated with lithium in the past. Although the lithium helped slightly with his irritability and mood swings, it did not decrease the hyperactivity or increase his attention. He felt "dull" and blunted when taking the lithium and stated adamantly that he did not want to take it again.

Adult ADHD, primarily hyperactive type, was diagnosed. After baseline pulse rate and blood pressure were recorded and baseline laboratory values were obtained, treatment was begun with a mixed amphetamine salt (Adderall) at a dosage gradually increased to 20 mg three times per day. He did well with the stimulant, which significantly decreased hyperactivity, irritability, and impulsive behavior. He reported improved job performance, and his wife and coworkers noticed a dramatic improvement in his attention, irritability, and task completion. He has continued Adderall therapy with no escalation of dosage and no evidence of medication abuse.

## **Case 2**

A 50-year-old man had a history of recurrent discrete episodes of significant depressive symptoms with depressed mood, poor concentration, lethargy, poor sleep, excessive worry, anhedonia, and suicidal ideation. Treatment with a combination of a paroxetine (Paxil) and mirtazipine (Remeron) had effectively ameliorated his depressive symptoms. Attempts to consolidate his regimen were not successful. Decreasing paroxetine resulted in an increase in his obsessive worry, and attempts to stop, decrease, or substitute for the mirtazipine caused a return of the depression. However, he had significant side effects from the medications, including sexual dysfunction, weight gain, and emotional blunting. He also continued to complain of ongoing poor concentration and continued to have difficulty holding a job. Despite having a graduate degree, he had difficulty keeping up with minimal paperwork requirements and frequently became overwhelmed when multiple demands were placed on him; during one such episode, he complained of thought disorganization, confusion, and intrusive suicidal ideation. At that time, he was given risperidone (Risperdal) in addition to paroxetine and mirtazipine. His thought disorganization and intrusive thoughts of suicide resolved.

When his depressive symptoms had abated and he had returned to his baseline mood, a more thorough developmental history was obtained. He reported a lifelong history of inattentiveness, distractibility, poor task completion, irritability, and chronic procrastination. He related his most severe episodes of depression to times in his life when he had been overwhelmed either at home, work, or school. He denied any history of hyperactivity or restlessness.

A tentative diagnosis of adult attention deficit disorder, primarily inattentive type, was made, and methylphenidate (Ritalin) was added to his antidepressant regimen. The patient described the immediate improvement as "life changing" in that he had an almost instantaneous improvement in concentration, task-completion, and job performance, with decreased worrying and distractibility. He also was referred for psychotherapy to help with his organizational skills. He

tapered and stopped the paroxetine therapy and currently continues to take mirtazipine (30 mg at night) and methylphenidate (20 mg three times per day). The sexual dysfunction, emotional blunting, and weight gain remitted. He has had no return of the obsessive worrying that occurred with previous attempts to stop taking paroxetine. He has remained at his current job for more than a year and has had no return of depressive symptoms.

## **Neurobiology**

There is substantial evidence of a brain metabolic deficit in children and adults with ADHD. In patients with ADHD, cranial computed tomography (CT) and magnetic resonance imaging (MRI) show no consistent pattern of structural abnormalities in adults or children that would be of significant benefit in diagnosis of ADHD. Nonetheless, several studies have indicated some variation in basal ganglia symmetry and in the corpus collosum in ADHD patients versus subjects without ADHD.<sup>[9]</sup> Studies using functional MRI and positron emission tomography (PET) have also shown evidence of abnormalities in patients with ADHD. In 1990 and 1993, Zametkin et al<sup>[10,11]</sup> found PET evidence of decreased brain glucose metabolism in the basal ganglia of ADHD adults and adolescents. A recent SPECT (single photon emission computed tomography) study of 10 adults with ADHD indicated increased striatal availability of a dopamine transporter; the availability diminished and specific binding decreased with methylphenidate therapy.<sup>[12]</sup>

Genetic studies offer the most convincing evidence of the biologic basis of ADHD. Twin studies show a higher rate of ADHD symptoms in monozygotic twins versus dizygotic twins of ADHD patients. Sibling studies show a higher incidence of similar symptoms in full siblings versus half siblings of ADHD patients.

Dopamine and norepinephrine have the best documented roles in attention and concentration. Stahl<sup>[13]</sup> implicates dopamine as mediating cognitive functions such as "verbal fluency, serial learning, vigilance for executive functioning, sustaining and focusing attention, prioritizing behavior, and modulating behavior based on social cues." He describes norepinephrine as playing a role in "sustaining and focusing attention, as well as in modulating energy, fatigue, motivation and interest."<sup>[13]</sup> Noradrenergic pathways project from the locus caeruleus to the frontal cortex, and dopaminergic pathways project from the brain stem to the prefrontal areas. These pathways are postulated to be mediators of arousal, attention, and concentration. Generally, medications that increase dopamine and norepinephrine transmission and availability seem to improve concentration and attention and thus decrease hyperactivity/impulsivity in ADHD adults and children.

## Comorbidity and Differential Diagnosis

As in children, there is a high level of comorbidity in adults with ADHD. Spencer et al<sup>[3]</sup> reported high rates of anxiety disorders (50%), substance abuse (27% to 47%), and antisocial personality disorders (12% to 27%). Because of the significant overlap with other psychiatric diagnoses, there has been speculation that ADHD could simply be a precursor to other psychiatric conditions as opposed to an independent entity. However, as Spencer et al<sup>[3]</sup> pointed out, if that were true, ADHD in adults would rarely be present without another diagnosis. In fact, approximately 40% of adults with ADHD will not have a coexisting anxiety, affective, or personality disorder but still have reported significant impairment.<sup>[3]</sup> Nonetheless, patients with adult ADHD often will visit their physician because of anxiety, panic attacks, depression, or substance abuse. Because ADHD is a disorder of attention and of prioritization, patients are often overwhelmed, depressed, anxious, and irritable. Similarly, anxious and depressed patients may appear scattered; however, important issues in diagnosis are whether onset of symptoms occurred during childhood and whether the concentration and attention difficulties preceded or followed the onset of the affective or anxiety symptoms. Higher educational achievement does not exclude a diagnosis of ADHD, but adults with ADHD often report having to work much harder than their classmates or having extraordinary difficulty when attention to detail or sustained attention is essential.

There is significant overlap between ADHD and bipolar disorder. In a study of 56 bipolar patients, Sachs et al<sup>[14]</sup> concluded that ADHD in children might identify children at highest risk for early onset of bipolar disorder. Hyperactivity in adults can mimic a manic episode; however, manic patients usually describe discrete episodes of increased spending, grandiosity, hyperreligiosity, or hypersexuality distinct from their baseline behavior. In contrast, ADHD patients generally report a chronic, ongoing difficulty with impulsive behavior, money management, and procrastination.

Substance abuse can be an effort to self-medicate the attention deficits, anxiety, or mood problems. The substances also can confuse the diagnosis, and their effects can mimic ADHD if the substance abuse is ongoing. Thus, the presence or absence of substance abuse and its temporal relationship to the difficulties in concentration and memory will need to be addressed if treatment is to be successful.

Again, a childhood history of ADHD symptoms is required to make the diagnosis in adults. New onset of difficulty in concentration, poor memory, and brief attention span are suggestive of diagnoses other than ADHD and warrant an organic workup and assessment for psychiatric or other medical causes. Medical diagnoses that could be manifested in a similar fashion include hyperthyroidism or hypothyroidism, seizure disorders, sleep apnea, drug interactions, hearing deficits, vitamin B12 deficiency, head injury, and heavy metal poisoning. Medical evaluation should include a neurologic examination and a mental status examination. Baseline laboratory studies might include thyroid function tests, vitamin B12 measurement, complete blood count, electrolyte and liver function

tests, and serum heavy metal screen. Baseline blood pressure determination and an electrocardiogram (ECG) should be considered if the patient has a history of hypertension or arrhythmia or if treatment with a stimulant or a tricyclic antidepressant is under consideration. If the attention and concentration problems are new in onset, cranial MRI or CT and an EEG might be considered as well.

## Treatment

Because there is significant comorbidity in adults with ADHD, coexisting depressive, anxiety, and substance abuse disorders will need to be addressed for treatment to be successful. If the ADHD symptoms are determined to be primary or if the other disorders are under adequate control, medication and behavioral treatment should be considered.

The stimulants are the most widely used medications to treat ADHD in children and have shown efficacy in adults as well. Recently, a study by Horrigan and Barnhill<sup>[15]</sup> showed some improvement in ADHD adults treated with a mixed amphetamine salt (Adderall). Predictably, some of the nonresponders had a comorbid anxiety disorder and had increased anxiety associated with use of the stimulant. Similarly, Paterson et al<sup>[16]</sup> also found some improvement in ADHD adults treated with dextroamphetamine. Methylphenidate (Ritalin, Concerta) has been a mainstay of treatment in children and has significant efficacy in adults as well. In a review of the literature, Spencer et al<sup>[3]</sup> found a response rate to methylphenidate in adults of between 25% and 75% in several controlled studies; this is significantly less consistent than the response rate of children but could be explained by a variety of factors, including psychiatric comorbidity, dose differences, and methodologic differences. A 1995 study of response to methylphenidate in adults with ADHD reported a 78% response rate.<sup>[17]</sup>

Pemoline (Cylert) has a mechanism of action similar to that of the stimulant medication and has the advantage of not being a schedule II controlled drug. However, pemoline should be used with caution because of the risk of hepatotoxicity. If pemoline is prescribed, baseline and regular liver function tests are essential. Methamphetamine rarely is prescribed because of its potential for abuse and its high "street value."

Several antidepressants have some efficacy in treating ADHD as well. The noradrenergic tricyclic antidepressants imipramine and desipramine have been reported to be effective in the treatment of ADHD in children and most likely have some efficacy in adults as well. The atypical dopaminergic and noradrenergic antidepressant bupropion (Wellbutrin) has had the most evidence of efficacy of the newer antidepressants. Several studies have indicated that bupropion could be useful in the treatment of ADHD in children. Barrickman et al<sup>[18]</sup> in 1995 and Connors et al<sup>[19]</sup> in 1996 also found efficacy for bupropion in the treatment of ADHD in younger patients. In addition, the selective serotonin and norepinephrine reuptake inhibitor venlafaxine (Effexor) has shown promise in the treatment of ADHD in several open trials in adults.<sup>[20-21]</sup>

The selective serotonin reuptake inhibitors generally are not thought to be useful in the treatment of core ADHD symptoms. They are often helpful, however, in ameliorating comorbid anxiety and affective complaints and should be considered for adjunctive treatment.

Choosing the appropriate medication option will depend on the psychiatric, medical, and substance abuse history of the patient seeking treatment. If the patient reports a history of a positive response to a particular medication as a child, it makes sense to try that medication for the adult. Comorbid depression or anxiety should be addressed, and a thorough history to rule out bipolar disorder is essential. Stimulants or antidepressants can exacerbate or precipitate a manic episode. If the patient has a history of substance abuse, especially abuse of stimulants, the primary care physician should be wary of prescribing a stimulant as first-line therapy. If stimulants are chosen as an option, one should monitor blood pressure, consider an ECG if indicated, and monitor for an increase in anxiety, agitation, or irritability in susceptible patients. Stimulants such as methylphenidate, dextroamphetamine, and the mixed amphetamine salt Adderall should be begun at low dosages of 5 to 10 mg two or three times per day and gradually increased as needed for improvement in concentration and attention. Patients should be warned that taking a stimulant later in the evening might cause difficulty sleeping, though some patients, because of the return of the core ADHD symptoms when the stimulant wears off, do report difficulty "settling down" to get to sleep if they do not take a dose later in the day. Stimulants sometimes can cause an exacerbation of comorbid tic disorders. Usually, any increase in abnormal movements will abate after the stimulant is discontinued, but exacerbation or unmasking of tic symptoms should prompt evaluation for an underlying Tourette's syndrome. When there is a positive response to the stimulants, patients often see an improvement in their core symptoms in a matter of days or even hours after beginning the stimulant medication.

If the stimulants are not effective or tolerated or if there is a contraindication to using them, antidepressants with a dopamine and/or norepinephrine enhancing mechanism of action are a viable option as well. While the onset of action is not as rapid or as dramatic, antidepressants such as bupropion, venlafaxine, or desipramine also can be used to treat comorbid depression and anxiety. Additionally, they are not schedule II drugs and have little or no potential for abuse.

Nonmedication interventions also are useful in the treatment of ADHD. Education about the disorder is important. Adults with ADHD often are relieved to find a name and a cause for their lifelong difficulties, and knowing the exact nature of their problem allows finding ways of coping more effectively. Examples of coping mechanisms for poor attention span or distractibility could include minimizing external distractions in the office or workplace, making lists, purchasing a computerized organizer, and establishing multiple small deadlines for finishing long-term projects. Patients with ADHD should be encouraged to educate themselves about the disorder and to consider joining support groups such as Children and Adults With Attention Deficit Disorder. Adults with ADHD should be

educated about the increased risk for substance abuse and the dangers of self-medication and should be strongly encouraged to minimize alcohol consumption. Also, referral to a therapist to help with organizational skills, prioritization, and anger management often is helpful.

Because patients with ADHD have difficulty with task completion, procrastination, and emotional outbursts, long-term damage to relationships can occur before diagnosis and treatment. Often, an unforeseen effect of successful medication and behavioral treatment is that it can change the "balance of power" in the relationship, prompting a conflict when the treated member of the relationship behaves in a less reactive and more proactive manner. Thus, education of the spouse or partner is important and referral for couples therapy sometimes is necessary during or after medication treatment.

## **Summary**

Once thought to be a disorder only of childhood, ADHD can and does persist into adulthood in a substantial percentage of patients. Childhood symptoms are a prerequisite for a diagnosis of ADHD in an adult. Because there is significant overlap with other disorders, a thorough developmental history, a substance abuse history, a medical and neurologic examination, and baseline laboratory studies are indicated to rule out other causes for poor attention and concentration. The Utah, Copeland, and Brown scales can be useful in making the diagnosis of ADHD in adults.

Medications that increase availability of dopamine or norepinephrine are most effective in the treatment of ADHD. Stimulants are the mainstay of treatment, but antidepressants with dopamine or norepinephrine agonist or reuptake properties also are effective and should be considered when stimulants are not effective or tolerated or when substance abuse is an issue. Nonmedical interventions such as education, support groups, and individual and couples counseling also are effective in improving response and decreasing comorbidity. If the diagnosis is unclear or if response to intervention is inadequate, referral to a psychiatrist or a psychologist is indicated.

Take time to deliberate, but when the time for action arrives, stop thinking and go in. -- Andrew Jackson

## **CME Information**

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## Disclosure

In publishing this section in Southern Medical Journal, the Southern Medical Association recognizes educational needs of physicians in all specialties, especially those in primary care, for current information regarding the diagnosis and treatment of attention deficit/hyperactivity disorder. In this section, authors may have included discussions about drug interventions, whether Food and Drug Administration approved or unapproved. Therefore, it is incumbent on physicians reading this section to be aware of these factors in interpreting the contents and evaluating recommendations. Moreover, views of authors do not necessarily reflect the opinions of the Southern Medical Association. Every effort has been made to encourage the author to disclose any commercial relationships or personal benefit that may be associated with this section. If the author disclosed a relationship, it is indicated below. This disclosure in no way implies that the information presented is biased or of lesser quality, but allows participants to make informed judgments regarding program content.

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### **Sidebar: Key Points**

- Diagnosis of attention deficit hyperactivity disorder (ADHD) in adults has as a prerequisite the presence of ADHD symptoms during childhood.
- Common adult ADHD characteristics include stubbornness, chronic conflicts with authority, difficulty in spouse and peer relationships, frequent job changes, poor frustration tolerance, and poor academic performance despite adequate or even superior intellectual abilities.
- Genetic studies offer the most convincing evidence of the biologic basis of ADHD.

- The stimulants are the most widely used medications to treat ADHD in children and have shown efficacy in adults as well.
- If the stimulants are not effective or tolerated or if there is a contraindication to using them, antidepressants with a dopamine and/or norepinephrine enhancing mechanism of action are a viable option as well.

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