

Continuing Education for Pharmacists



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ADHD and Its Treatment in Adults

Goal. The goal of this lesson is to explain attention-deficit/hyperactivity disorder (ADHD) in adults with focus on its clinical characteristics and confirmation, and its treatment.

Objectives. At the conclusion of this lesson, successful participants should be able to:

1. recognize epidemiologic information and characteristics relevant to ADHD;
2. identify symptomatology that characterizes ADHD and the principles that govern its clinical confirmation and management in adults; and
3. select from a list specific nonpharmacologic and pharmacologic measures that are reported to modify signs and symptoms of ADHD in adults.

Attention-deficit/hyperactivity disorder (ADHD), which affects up to 12 percent of children and adolescents, persists into adulthood in up to 60 percent of cases. Four to 5 percent of adults worldwide are affected, making ADHD one of the most common psychiatric conditions in adulthood for which treatment is available.

Only recently has the persistence of untreated ADHD in adults been recognized in primary care. Marked by inattention, distractibility and impulsivity, clinical features of adult ADHD are reminiscent of the symptoms of childhood ADHD; however, the condition evolves and changes as the individual matures.

Work productivity loss in adults with ADHD is estimated at 35 days each year. Annual health care costs for adults with ADHD, compared with an age-matched cohort of unaffected adults, are three times higher, and annual health care expenditures for their family members are approximately 1.9 times higher compared with a matched cohort (group consisting of shared characteristics) of family members of non-ADHD patients.

Background

In adults, ADHD can lead to substantial social and occupational impairment and is associated with increased familial stress. Fewer adults with ADHD are employed full time, indicating that those with ADHD have a lower average income than control subjects, regardless of academic achievement or personal

characteristics.

Adults with ADHD have been shown to be more careless drivers, and more likely to receive multiple citations for speeding and have their driver's license revoked. Adults with ADHD are twice as likely to have been arrested and convicted of a crime.

Only 47 percent of adults with ADHD report being satisfied with their family life, compared with 68 percent of those without the condition. Adults with ADHD are twice as likely to be divorced. Only half of affected adults report contentment with their professional life.

Adolescents with and without ADHD have the same rate of substance abuse; such is not the case for adults with ADHD. Between adolescence and adulthood, the rate of substance abuse increases substantially for individuals with ADHD.

Although parents may worry that treating ADHD with psychostimulants will predispose their children to substance abuse later in life, treatment may actually protect against the development of substance abuse. If ADHD is consistently and effectively treated during the childhood and adolescent years, the risk of substance abuse

Table 1
Top ten symptoms of adults with ADHD that lead to self-referral to a physician

1. Poor concentration
2. General disorganization
3. Tendency to leave projects incomplete
4. Inattention
5. Poor school performance
6. Problems with time management
7. Difficulty controlling temper
8. Impulsive
9. Anxiety
10. Difficulty functioning at work

Adapted in part from Faraone SV, Spencer TJ, Montano B, Biederman J. Arch Intern Med. 2004;164:1221-1226.

later in life is no greater than in the general population.

ADHD may affect sexual behavior. The Milwaukee Young Adult Outcome Study showed that sexually transmitted disease was four times more prevalent among persons with ADHD than their non-affected peers. Affected persons also had far more children by age 20, but only half of the ADHD parents retained custody of their children.

Executive functioning (the ability to maintain appropriate problem solving activity for attainment of a future goal) is an area of intense research in the study of ADHD. Problems present clinically as deficits in time management, organization, and sequential and hierarchical thinking. Exceptionally intelligent adults are often able to compensate for their inabilities through adolescence and even young adulthood, but the cumulative challenges may eventually overwhelm their compensatory mechanisms.

Data describing the likelihood that a child with ADHD will also have the disorder as an adult are conflicting. As definitions of ADHD subtypes improve, some subtypes will likely be found that cause more adult dysfunction than others.

Pathogenesis

As in childhood and adolescent ADHD, the most critical neurotransmitters in adults with ADHD are the catecholamines dopamine and norepinephrine, both of which appear to regulate inhibitory influences in the frontal-cortical processing of information. Specific neurobehavioral roles for these neurotransmitters remain unclear. Both dopamine and norepinephrine act upon relatively specific pathways that regulate attention, concentration and other cognitive functions. It is theorized that dopamine enhances signals and improves attention, acquisition, focus, on-task behavior and cognition, perception and vigilance. Norepinephrine may diminish “noise;” decrease distractibility and shifting; improve executive operations; and increase behavioral, cognitive, and motor inhibition. In terms of pathophysiology, it is postulated that neurotransmitter dysfunction causes dysregulation of the inhibitory influences of frontal-cortical activity, which is predominantly regulated by norepinephrine, and of lower striatal structures, which are predominantly dopaminergic. These striatal structures are driven by dopaminergic agonists controlled or modulated by higher inhibitory structures sensitive to adrenergic agents.

Clinical Confirmation in Adults

There are no efficient standardized assessment tools to specifically identify adult ADHD, which makes diagnosis confirmation challenging. Extensively studied in children, its persistence into adulthood was not recognized until the mid-1970s. These symptomatic adults were diagnosed retrospectively with ADHD following interviews with their parents and determination that symptoms of illness characteristic of the disorder had indeed been noticed during the affected adults’ early years.

Current guidelines for both children and adults are that patients must meet the criteria established by the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSMIV). Symptoms are categorized as follows: inattention (difficulty sustaining attention), forgetfulness and distractibility; hyperactivity (fidgeting, excessive talking and restlessness) and impulsivity (difficulty waiting one’s turn and frequent interruption of others). The DSM-IV criteria also include onset by age seven (confirmed, possibly, by retrospective analysis), impaired functioning in at least two settings (home, work, school), and persistence beyond six months. Symptoms.

Symptoms in adults are similar to those in childhood except they are usually less disruptive and more along the lines of a sense of inner restlessness. Typically, adults with ADHD are unaware that they have the disorder. They may feel it is difficult to get organized, to stick with a job or keep an appointment. Everyday tasks of arising in the morning, getting dressed and ready for the day’s work, arriving at work on time and being productive on the job can be major challenges for the ADHD adult. Problems may intensify in adulthood when they begin an independent life with increasing challenges for organization associated with marriage, parenting, occupational planning and administration.

Adults almost always self-refer for treatment rather than having a physician suggest its presence initially. This may occur when their children are diagnosed with the disorder and they begin to understand that some of the traits that have troubled them for years might point to ADHD as the root cause of their problems. Other adults seek professional help for anxiety or other symptom(s) listed in Table 1. They may have a history of social inadequacy or problems at work, or

they have been involved in frequent automobile accidents and they seek answers for the root cause of their "problem." Gender distribution of self-referring adults is nearly equal.

A presenting comorbidity (concomitant, but unrelated illness) may be the first clue to the presence of adult ADHD. The majority of adults with ADHD have at least one additional psychiatric disorder such as anxiety, bipolar disorder or major depressive disorder; some adults may have more than one. Because there is considerable symptom overlap, this creates the potential for diagnostic confusion with consequent tendency to disguise a diagnosis of ADHD. It is also possible that many adult patients with ADHD have clinically significant but subthreshold symptoms.

Hyperactivity symptoms may decrease with age because of developmental trends toward self-control. Adults with ADHD are generally less hyperactive than children. Whereas young children can often be seen in purposeless climbing, jumping and running about, adult variants of these characteristics include such traits as being a workaholic, feeling uncomfortable sitting through meetings or a movie, being unwilling to wait in line, and speeding while driving. Affected adults often work overtime and/or hold more than one job. Symptoms of hyperactivity in adults may also be based not so much on motor behavior but on other aspects of functioning, such as talking. Adults may feel they need to talk excessively or they regularly talk out of turn, blurt out inappropriate comments, or feel compelled to talk endlessly on their cell phone during meetings or while driving. Such behaviors can lead to both personal and professional harm. Inattentive symptoms do not appear to have a similar developmental advantage and they tend to remain constant throughout adulthood.

Adults with ADHD may be unable to understand which of their actions provoke irritation in others, but

advancing age does have an advantage in that they may have better insight into monitoring the reactions of others and so they adjust their behavior accordingly. Traits that were problematic in childhood may be adaptive to selective jobs by an adult. This does not imply that these adults no longer suffer impairment in quality of life, social relationships, personal planning, underemployment, motor vehicle safety and other dimensions of functioning. As one adult wisely said, "You don't grow out of ADHD; you just get better at coping with it!" It stands to reason that adults with ADHD experience life differently from persons without ADHD.

Treatment

Pharmacotherapy of adult ADHD is an effective means to manage symptoms of the disorder, with approximately two-thirds of adult patients experiencing moderate-to-marked improvement with drugs when combined with psychoeducational management. Clinical trials have confirmed that medications positively improve core ADHD symptoms by enhancing levels of dopamine and/or norepinephrine.

Stimulants. The two major stimulant categories used to treat ADHD are the amphetamines and methylphenidates, compounds with a similar clinical effect. Stimulants comprise the majority of treatment protocols for both children and adolescents, and for adults. Seventy-five to 80 percent of adults with ADHD responded positively to stimulants in short-term trials. It is reported that 1.5 million adults in the United States now take stimulants on a daily basis to treat their ADHD, with 10 percent of users older than 50 years of age.

Amphetamines include dextroamphetamine (d-amphetamine; Dexedrine, etc.) and mixed amphetamine salts (Adderall, etc.). Recent advances have occurred with delivery systems rather than new and novel drugs. Long-acting formulations allow for

more convenient and confidential administration of medication and eliminate the possibility of forgetting to take midday doses. They also reduce peak and trough adverse effects such as headache and moodiness, and eliminate afternoon wear-off and rebound. An extended-release form of mixed amphetamine salts (Adderall XR) provides 10 to 12 hours of activity. Lisdexamfetamine (Vyvanse), approved in 2007 for use in children, may become another alternative therapy for adults. Lisdexamfetamine is composed of d-amphetamine combined with the amino acid lysine that renders the molecule inert. Gastric enzymes cleave the lysine, which activates the molecule. Since gastric enzyme exposure is necessary for activation, this ensures that the medication cannot be misused if snorted or injected intravenously. Lisdexamfetamine is also long-acting and has consistent pharmacodynamic properties.

Methylphenidate is available in immediate-release (four-hour duration of action), longer acting (six- to eight-hour duration), and extended-release (10- to 12-hour duration) formulations. Osmoticrelease oral system (OROS) methylphenidate (Concerta) releases the active ingredient slowly over 12 hours. Dexmethylphenidate (Focalin) is comprised solely of the dextro-(active) portion of the methylphenidate molecule. Products are available in immediate and extended-release formulations. The methylphenidate transdermal system (Daytrana) is an alternative to orally-administered drugs that delivers the active ingredient via skin patch. With optimal wear time of nine hours each day, its duration of action persists up to three hours after the patch is removed.

Adverse effects of stimulants are generally mild and can be managed by adjusting the medication timing and dosage. The most common short-term effects are diminished appetite, GI disturbance, headache, insomnia and motor disturbance.

Table 2
Helpful websites for adult ADHD*

www.cdc.gov	Centers for Disease Control and Prevention
www.chadd.org	Children and Adults with Attention-Deficit/Hyperactivity Disorder
www.nami.org	National Alliance on Mental Illness
www.nimh.nih.gov	National Institute of Mental Health

**Enter Adult ADHD and search.*

Non-stimulants. Atomoxetine (Strattera) is a highly selective norepinephrine reuptake inhibitor in presynaptic neurons; it reduces reuptake of dopamine in prefrontal lobes to a lesser extent. It is of interest that development of atomoxetine was initially piloted in adults rather than children, although confirmation of benefit in children followed. At present, it is the only non-stimulant with FDA approval for treatment in adults. It often takes longer than the stimulants to achieve clinical effect, but has a powerful anxiolytic effect and minimal abuse potential. Atomoxetine is generally well tolerated with few mild side effects including appetite suppression and insomnia.

Antidepressants are considered a second choice for treatment of adults with ADHD following a trial with the stimulants and atomoxetine. The older antidepressants (tricyclics) are sometimes used because they modify norepinephrine and/or dopamine. Venlafaxine (Effexor), a non-tricyclic antidepressant, is also used for its enhancement effect on norepinephrine. Bupropion (Wellbutrin, etc.), an antidepressant with an indirect effect to increase central dopamine, has been useful in treatment of ADHD in both children and adults. It has the added benefit of aiding reduction of nicotine dependence.

Education and Psychotherapy. Although pharmacotherapy provides needed support, the individual must succeed on his own. To assist in this struggle, both education and individual psychotherapy can be helpful. Adults can learn how to organize their life by posting a large

calendar where it will be seen each morning that lists important tasks for the day. A special place can be set aside for keys, bills and the paperwork of everyday life. Tasks can be organized into segments such that completion of each part can give a sense of accomplishment. Above all, adults with ADHD should learn as much as they can about their disorder so they understand what is going on in their body and, thus, be better equipped to manage it.

Psychotherapy can be a useful adjunct to medication and education. Therapy can help patients improve their poor self-image by examining experiences that produced it. The therapist can encourage patients to adjust to changes in their life by treatment - the loss of impulsivity and desire for risk-taking, and the new feeling of thinking before acting. As patients begin to understand their new ability to organize the complexities of life, they can often begin to appreciate characteristics of ADHD that are positive, such as new-found energy, warmth, and enthusiasm.

Focused therapies that incorporate cognitive-behavioral features have reportedly been effective in children, adolescents and adults with ADHD. The benefit of these treatments without concurrent pharmacotherapy has yet to be determined.

Drug Holidays. Drug holidays, common in treatment of childhood ADHD, may also become part of the pharmacotherapy of adult ADHD. However, there is growing consensus that this practice of withholding medication one or more days each week in adults is inappropriate and

that medication is most effective when taken consistently without interruption.

Adherence. Poor adherence with treatment is common in the care of adult patients initiating stimulant therapy. In one study, adults initiating pharmacological treatment for ADHD continued their medications for an average of only 50 days. Although early discontinuation of treatment commonly occurs in the care of adult ADHD, the factors that promote continuity of stimulant treatment remain largely unknown.

Optimal management of ADHD includes pharmacologic and nonpharmacologic interventions. Support groups help persons of all ages with ADHD and their family members understand the disorder and available resources. Support groups can be located by calling an ADHD hotline (800.233.4050) or by contacting Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD) (Table 2). Other helpful websites on ADHD are also listed in Table 2.

Summary and Conclusions

Adult ADHD is one of the most common psychiatric disorders. It differs from ADHD in children and adolescents in that adults can often modify their daily routines to better match their temperament. It has been shown in most clinical trials that pharmacologic treatments effective in children and adolescents are also effective in adults. Although adults with ADHD are at higher risk for substance abuse than adults without the disorder, recent studies have shown that pharmacotherapy may reduce the risk of substance abuse in adults with ADHD.

The content of this lesson was developed by the Ohio Pharmacists Foundation, UPN: 129-000-08-009-H01-P. Participants should not seek credit for duplicate content.

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1. Work production loss in adults with ADHD is estimated at:

- a. 15 days each year.
- b. 35 days each year.
- c. 55 days each year.
- d. 75 days each year.

2. Between adolescence and adulthood, the rate of substance abuse for individuals with ADHD:

- a. increases.
- b. decreases.

3. The most critical neurotransmitters in adults with ADHD are dopamine and:

- a. acetylcholine.
- b. gamma-aminobutyric acid.
- c. norepinephrine.
- d. serotonin.

4. Which of the following is NOT listed as a function regulated by dopamine and/or the neurotransmitter referred to in question # 3?

- a. Concentration
- b. Attention
- c. Perception
- d. Memory

5. Which of the following statements is true?

- a. Adults almost always self-refer for treatment of ADHD.
- b. Physicians almost always suggest the presence of ADHD in adults initially.

6. Which of the following statements is most likely to be true about adults with ADHD?

- a. They understand which of their actions provoke irritation in others.

- b. They are not able to adjust their behavior to the reaction of others.
- c. They do not suffer impairment to quality of life or social relationships.
- d. Traits that were problematic in childhood may be adaptive to selective jobs.

7. The percentage of adults with ADHD who responded positively to stimulants in short-term trials has been:

- a. 55 to 60 percent.
- b. 65 to 70 percent.
- c. 75 to 80 percent.
- d. 85 to 90 percent.

8. Which of the following products is comprised solely of the dextro- (active) portion of the methylphenidate molecule?

- a. Strattera
- b. Focalin
- c. Dexedrine
- d. Concerta

9. Which of the following products is a non-stimulant drug?

- a. Strattera
- b. Focalin
- c. Dexedrine
- d. Concerta

10. There is growing consensus that the practice of withholding ADHD medication one or more days each week in adults is:

- a. appropriate.
- b. inappropriate.



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Volume XXVI, No. 9
GPhA Code J09-01
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