Supplement to Psychiatric Times

Reporter

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Educational Objectives

Upon completion of this activity, the learner will be able to:

- Identify the ways in which current *DSM-IV* criteria present challenges for the diagnosis of adolescents and adults with ADHD.
- Describe at least two areas of functional impairment that are markedly present in adolescents and adults diagnosed with ADHD.
- Review and apply the medication options for the treatment of ADHD in adults.
- Review and assess the treatment considerations for adult ADHD and concurrent comorbid psychiatric disorders.

Who will benefit?

This activity was designed to meet the continuing education needs of psychiatrists and other physicians, physician assistants, registered nurses, and advanced practice psychiatric nurses. Other mental health professionals may find this activity informative and should check with their state licensing and certification boards to determine if it meets their continuing education requirements.

Disclosures

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Improving Functional Outcomes in Adolescent and Adult ADHD: Efficacy and Safety of Pharmacologic Therapies

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Understanding the Challenges in the Diagnosis of Early and Late Adolescent and Adult ADHD

by Scott H. Kollins, PhD

Attention-deficit/hyperactivity disorder is one of the most common psychiatric disorders and is estimated to affect approximately 8% of children and adolescents in the United States.[1] It is now well established that in many cases, the symptoms and impairment associated with ADHD persist into adulthood, resulting in prevalence estimates of 4.4% for adults in the United States.[2] The common occurrence of ADHD in children and adolescents is also recognized throughout the rest of the world, with a recent meta-analysis estimating the worldwide prevalence as 5.3%.[3] Considering these prevalence estimates, it is surprising that ADHD is widely undertreated, with only 50% of children/adolescents and 10% of adults diagnosed with ADHD actively receiving treatment.[2,3] Perhaps relating to these low rates of treatment, ADHD is associated with a wide range of functional impairments, including lower academic achievement, higher divorce rates, lower occupational/vocational achievement, increased risk for psychiatric comorbidity, increased risk of arrest or incarceration, increased risk for accidents and emergency department visits, and increased risk of traffic accidents and violations.[4-8] These impairments lead to staggering costs to society. Recent estimates suggest that the direct and indirect costs of ADHD are as high as $15,000 per patient, which adds up to tens of billions of dollars annually, when overall prevalence estimates are considered.[9-11] Given the impairments caused by ADHD and their subsequent costs to society, it is critical to consider in detail some of the diagnostic challenges presented by this disorder, especially as patients age into adolescence and adulthood.

Diagnostic Challenges

It is critical to accurately assess and diagnose ADHD in adolescents and adults. However, there are a number of challenges facing clinicians who are likely to see ADHD patients in their practices. First, from a training perspective, many, if not most clinicians do not receive explicit training in assessing or treating ADHD in patients older than 12 or 13. This is related to the historical conceptualization of ADHD as a disorder of childhood. As such, general adult psychiatrists or psychologists are typically forced to learn about ADHD in older patients through direct experience and trial and error. Another challenge facing clinicians pertains to the standard criteria used for making a diagnosis. The *DSM-IV* criteria for ADHD were, for the most part, rigorously and empirically developed, though primarily for children.[12] As a result, aspects of the criteria are developmentally inappropriate for standard assessment with adults. Several of the symptom criteria are not applicable to adults such as "runs about and climbs on things excessively" or "has difficulty playing or engaging in leisure activities quietly." In addition, the assessment of childhood symptoms is usually difficult, especially for older adults. However, it is critical to establish the presence of symptoms in childhood even if the specific *DSM-IV* age of onset is considered to be somewhat arbitrary.[13]

It can also be challenging to assess whether symptoms of ADHD are present in multiple domains. When assessing children, it is clinical convention to get objective behavioral ratings from parents and teachers. However, the approach to assessing symptoms across settings in adults can be hindered by the fact that many adults may not want people at work, or even family members, know that they are seeking assessment. Finally, the presence of comorbid conditions makes differential diagnosis in adults potentially even more difficult than in children. Adult patients have reached the age of risk for a wide range of comorbid conditions and accurately distinguishing ADHD from mood, anxiety or substance use disorders or other problems complicates assessment efforts. The **Table** summarizes some of the diagnostic challenges posed by current *DSM-IV* criteria for the assessment of adolescent and adult ADHD.

Complicating the diagnostic picture further are data from several sources suggesting that even adults who fail to meet full ADHD criteria experience considerable functional impairment. Faraone et al.[14] studied a sample of 247 individuals with variations of ADHD and a control group of 123 individuals. The variations of ADHD included a full diagnosis (N=127), those meeting all criteria except for the age of onset prior to age 7 (N=79) and those not meeting full symptom criteria (i.e., fewer than six symptoms from one or both of the Inattention or Hyperactive-Impulsive domains; N=41). Results showed that across all three of the clinical groups, individuals experienced more functional

impairments compared to the control group (e.g., more academic tutoring, have ever been arrested, more speeding tickets). Moreover, individuals who met all criteria except the age of onset appeared similar to the full criteria group for other problems.

Fortunately, in the past few years, considerable effort has gone into developing valid and reliable approaches to assessing adults and adolescents with ADHD. This has led to the development of several rating scales that can be used by patients themselves and significant others to assess the presence of symptoms. The Conners' Adult ADHD Rating Scales (CAARS) has extensive norms and good psychometric properties, and is available in self-report and observer versions.[15] The CAARS has been used for many adult clinical trials for ADHD. Other validated measures for symptom assessment in adults with ADHD are also available. A six-item screening measure (Adult ADHD Self-Report Scale [ASRS]) has been developed that shows good internal consistency and concurrent validity.[16] A measure such as this is best used to identify patients who may benefit from more thorough diagnostic assessment.

Progress has also been made in the development of psychometrically sound interviews that address the other *DSM-IV* criteria for ADHD. The Conners' Adult ADHD Diagnostic Interview for *DSM-IV* (CAADID) has been shown to have good test-retest and inter-rater reliability, and corresponds to other measures of ADHD symptoms and impairment.[17] Tentatively scheduled for publication in 2011, *DSM-V* will hopefully address some of the specific challenges inherent in the present version with respect to diagnosing adolescents and adults. In a similar manner, guidelines are needed that address practice parameters for assessing (and treating) adults with ADHD. Such guidelines are available for children, but not explicitly for adults.[18]

Table ***Diagnostic Challenges Posed by DSM-IV ADHD Criteria When Assessing Adolescent and Adult Patients***

DSM-IV Criterion	Diagnostic Challenges
A) Symptom criteria	• Many symptoms not developmentally appropriate [illegible] adults: [illegible] runs about/climbs on things excessively; difficulty playing quietly
B) Some symptoms were present and caused impairment prior to age 7	• Adult patients not able to reliably recall behavior at this young age • Difficulty [illegible]
C) Some impairment present in ≥2 settings	• Difficulty gathering reliable information from multiple settings (work, home, social, etc.)
D) Clear evidence of clinically significant impairment	• In some cases impairment may be harder to assess compared to children
E) Symptoms are not better explained by another mental disorder	• Patients with [illegible] make ruling out alternative diagnoses much more difficult

Source: [illegible]

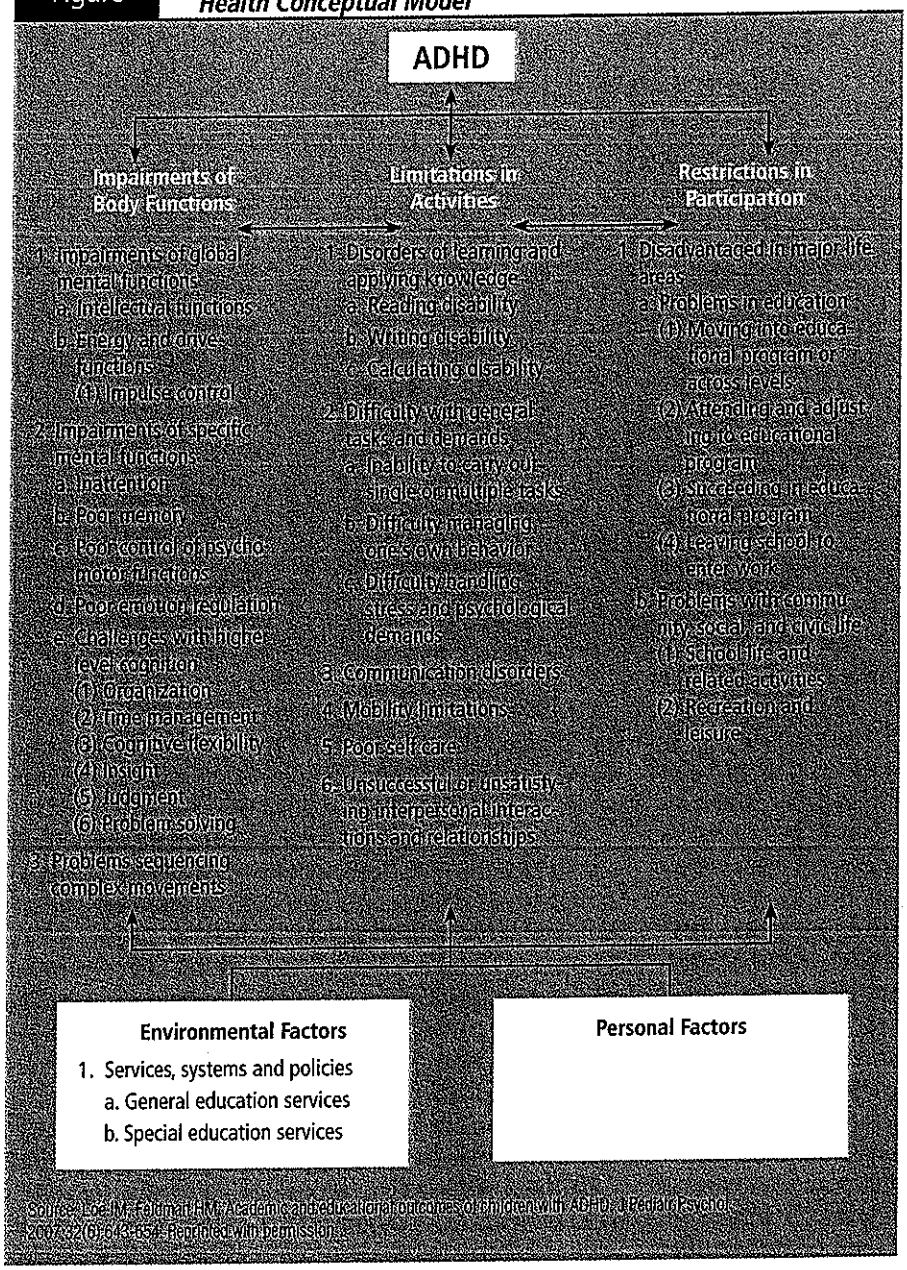
Functional Impairments

Clinically, we know that the reasons patients with ADHD seek treatment are often only indirectly related to the core symptoms of the disorder. That is, patients do not complain about deficits in attention or increases in activity level or impulsivity in an abstract sense. Rather, they complain about a wide range of functional impairments, which are how the core symptoms interact with the day-to-day experiences of the individual patients. These impairments are typically the focus of our interventions and it is therefore important to consider some of the more commonly measured problems we see in older patients with ADHD.

The concept of functional impairment, though widely recognized, has not been objectively measured in clinical trials of ADHD until recently. This is due, in part, to the highly individualized nature of impairments. The manner in which core symptoms affect patients varies considerably, making measurement in studies challenging. One approach to indirectly measuring functional impairment has been to assess the construct of quality of life (QoL), which assesses the extent to which a disorder negatively affects an individual's life, oftentimes in comparison to other disease states. Quality of life has been assessed in a number of recent studies with ADHD samples. Several scales are available to assess this construct in both pediatric and adult populations. A number of studies have shown children with ADHD experience significantly worse QoL compared to children without ADHD, and that their QoL is comparable to other chronic diseases, such as cerebral palsy or cancer.[19-21] In adults with ADHD, measures are also available to measure QoL (e.g., ADHD Impact Module for Adults [AIM-A]).[22]

Interestingly, treatment studies in children, adolescents and adults have not always shown a high correlation between symptom reductions and changes in QoL, suggesting that the construct of QoL is not

Figure ***Functional Problems Associated With ADHD Using the International Classification of Functioning, Disability, and Health Conceptual Model***



Source: Loe IM, Feldman HM. Academic and educational outcomes of children with ADHD. J Pediatr Psychol. 2007;32(6):643-654. Reprinted with permission.

completely isomorphic with severity of ADHD symptoms.[23-26] These findings underscore the importance of assessing QoL and functional impairments on an individual basis in patients with ADHD. The association between ADHD and various domains of functioning is illustrated in the **Figure** and highlights how the disorder can interfere with a wide range of activities across the life span.[27]

Several specific impairments that are consistently associated with adolescent and adult ADHD are worth highlighting since they result in even greater levels of dysfunction and cost to society.

ADHD and SUDs

Prospective longitudinal studies indicate that individuals with a diagnosis of ADHD during childhood or adolescence are at increased risk for developing substance use disorders (SUDs) later in life, including dependence on both alcohol and illicit drugs.[7,28] In one longitudinal study, a four-year follow-up of patients between the ages of 6 and 17 with a baseline diagnosis of ADHD demonstrated that individuals with ADHD were more likely than non-ADHD controls to meet clinical diagnostic criteria for all SUDs examined, including alcohol, tobacco and drug dependence.[28]

The results of a number of cross-sectional surveys provide further evidence of a link between ADHD and the presence of SUD.[29-32] In a population-based study of all children in Olmsted County, Minn., adolescents with a childhood diagnosis of ADHD were 6.2 times more likely to have documented SUD before age 18 (21.9%) than matched controls (4.4%) ($P<0.001$).[31] In a study of familial ADHD, parents of children with ADHD who also met criteria for persistent ADHD exhibited comorbid SUD at a rate of 47%, a significantly higher rate compared with matched parents who did not have ADHD (28%).[32]

In addition to conferring risk for lifetime presence of substance use problems, ADHD also significantly impacts the course of SUD throughout the life span. Wilens et al.[33] demonstrated that the average age of onset of SUD was significantly younger in a sample of adults with ADHD compared to control adults. Most of the studies reviewed to this point have focused on alcohol and other drug use. Attention-deficit/hyperactivity disorder has also been shown to be a significant risk

factor for smoking and nicotine dependence, which is arguably an even more significant public health concern. Both adolescents and adults with ADHD smoke at rates that are significantly higher than the general population and, like other SUDs, age of onset of smoking tends to be younger among patients with ADHD than non-ADHD individuals.[34-38]

Other studies show that among patients with known SUD, a higher rate have ADHD diagnosed than would be expected in community samples. For example, in one study, 35% of adults presenting for treatment of cocaine addiction met the diagnostic criteria for ADHD, a rate roughly eight times higher than those seen in broad community epidemiologic surveys.[39]

ADHD and Depression

Depression is another common and impairing comorbidity often seen in adult patients with ADHD. In the recent National Comorbidity Survey Replication, 38.3% of all adults with ADHD were also diagnosed with a significant mood disorder, including major depression (18.6%), bipolar disorder (19.4%) or dysthymia (12.8%).[2] Conversely, in patients with mood disorders, ADHD occurred more frequently than what is observed in the general population (4.4%). Attention-deficit/hyperactivity disorder occurred in 9.4% of patients with major depression, 22.6% of patients with dysthymia and 21.2% of patients with bipolar disorder. These figures also do not take into account the substantial rates of subthreshold mood disorders often observed clinically that are secondary to ADHD. That is, adult patients who have grown up living with their ADHD-related impairments often experience decreased self-confidence/self-esteem that affect functioning, but might not meet full criteria for depression or dysthymia. Surprisingly, very little research has been done on effectively treating depression or ADHD in the context of one another, although several open-label trials have been conducted and additional efforts are under way.[40-42]

ADHD and Driving Impairments

Another unique and highly significant functional impairment affecting adolescents and adults with ADHD are deficits in driving performance. This should not be surprising given the level of attentional control necessary to safely and effectively operate a motor vehicle. Longitudinal and retrospective studies have repeatedly shown adolescents and adults with ADHD are at significantly greater risk for a wide range of adverse driving outcomes compared to matched controls. These outcomes include speeding tickets, accidents, license revocations and injury-related accidents.[43] Simulator studies have also shown driving impairments in patients with ADHD to be the result of inattention and greater effects of fatigue.[44,45] Fortunately, there is considerable evidence showing that proper pharmacological treatment of ADHD can reduce the driving impairments observed in these patients.[46,47]

Conclusion

Although long regarded as a disorder of childhood, the persistence of ADHD through adolescence and adults is now irrefutable. Clinicians face a wide range of challenges when assessing and diagnosing ADHD in older patients. Some of these difficulties are related to the nature of the current *DSM-IV* criteria, while others are related to some of the unique functional impairments experienced by adolescents and adults with ADHD. Future research into how these impairments develop as well as revisions to the *DSM* and subsequent development of reliable and valid instruments will hopefully aid clinicians in addressing these myriad challenges.

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Evaluating Treatment Strategies in the Management of Early and Late Adolescent and Adult ADHD

by David W. Goodman, MD

Although treatment guidelines for attention-deficit/hyperactivity disorder have been developed and published for children and adolescents,[1-3] there are none for ADHD in adults. The issue of concurrent psychiatric comorbidities in older adolescents and adults with ADHD complicates the development of treatment algorithms. The amount of research for adolescents with ADHD and psychiatric comorbidities is greater than for adults, but the overall paucity of such published research provides limited guidance.

Medication options to treat ADHD have demonstrated convincing evidence of efficacy across all ages. The agents are categorized into FDA-approved agents, stimulants (methylphenidate and amphetamine preparations) and nonstimulants (atomoxetine [Strattera]), and non-FDA approved agents (bupropion [Wellbutrin], desipramine [Norpramin], α-agonists, modafinil [Provigil] and venlafaxine extended-release [XR] [Effexor XR]). Medications for ADHD are approved for the disorder and age group of patients; so a stimulant preparation may be approved for children but not yet for adolescents or adults or a stimulant may be approved for children and adults but not yet for adolescents. The approval process rests on the submission of clinical research data in a specific age population.

However, it is generally accepted that an effective medication for ADHD will be useful for patients regardless of age. Efficacy rates for stimulants are generally reported to be similar in adults and children when using equivalent dosing.[4] Controlled trials in adults reported statistically significant improvement with stimulants compared with placebo, and response rates of 55% to 78% were seen using standard rating scales.[4-8] However, safety considerations may differ depending on the age of the patient, for example, the risk of sudden death in children taking stimulants versus hypertension in adults taking stimulants. Therefore, the FDA review process considers three factors for approval in a specific age population: efficacy (how well it works), tolerability (side-effect profile) and safety (serious or dangerous adverse events).

The constellation of symptoms in adolescents with ADHD resembles childhood core symptoms. Except for substance abuse, the psychosocial adversity and psychiatric comorbidity with mood and anxiety disorders appear identical.[9,10] Therefore, adolescents have often been included in childhood ADHD clinical trials. Generally, medications effective in children with ADHD show a similar level of efficacy in adolescents with ADHD.

Stimulants

A PubMed search conducted in August 2007 for adult ADHD medication trials found nine trials for amphetamine-based drugs and 19 trials for methylphenidate. Of the nine amphetamine trials (N=1483), six were double-blind and placebo-controlled. All nine trials were positive. Three had crossover designs and three had comparator agents. Of the 19 trials with methylphenidate (N=1292), 18 were positive. Sixteen trials were double-blind and placebo-controlled with 10 designed as crossover and one with a comparator. Although the number of adult studies pales in comparison to the child and adolescent literature, the trial numbers are growing with an increasing focus on the adult population with untreated ADHD.

Patients treated with stimulant medications may experience mild-to-moderate adverse events such as insomnia, gastrointestinal (GI) upset, decreased appetite, mild weight loss, headaches, dry mouth, constipation, hand tremors and jitteriness. During the course of a research study, participants are asked in general terms how they have been feeling since the last research visit. There are several shortcomings in the data resulting from this method of collection. First, adverse events tend to be underreported with spontaneous reporting and, therefore, these findings should be interpreted accordingly. Also, the timing of the reported adverse event in relationship to dosing is often not asked. Some side effects occur shortly after dosing while others occur as a wearing-off effect hours later. This information is not gathered in a clinical trial and leads to difficulty in interpreting the medication adverse-event profile.

An interesting finding in several adult ADHD trials is that there appears to be no dose relationship to specific adverse events (mixed amphetamine salts XR [Adderall XR],[7] dexmethylphenidate XR [Focalin XR],[6] OROS methylphenidate [Concerta][11] and lisdexamfetamine [Vyvanse]).[12] This finding from group data is counterintuitive to clinicians who assume the higher the dose the more likely the side effects. Although this may be true for a specific patient, it appears not to be true for the groups of patients with ADHD in these trials. Stimulant-naïve patients may be more sensitive to new side effects than patients who have been previously treated.[7,13] In addition, some side effects diminish with time while others do not. Side effects that do not diminish are often tolerated or treated palliatively (e.g., dry mouth or constipation).

Nonstimulants

In the nonstimulant category, the only FDA-approved medication for ADHD in adults is atomoxetine. There are nine published trials in adolescents as of 2006[14] and four published trials in adults.[15-17]

Bupropion has been studied in adults with ADHD and there are four trials, two of which were double-blind and placebo-controlled. The four adult trials (N=257) were all positive. There are no crossover or comparator trials in adults.[18] A single open-label trial in 36 adults with ADHD and treated comorbid bipolar disorder (BD) demonstrated significant improvement in ADHD symptoms without activation of mania.[19] A single double-blind, placebo-controlled trial of desipramine in 41 adults with ADHD had a positive outcome compared to placebo.[20] Guanfacine (Tenex), an α-agonist, has been studied in a controlled trial in adults and demonstrated a positive outcome on the *DSM-IV* Adult Behavior Checklist for Adults (ABCL) over placebo ($P<0.05$).[21] This small collection of research in adult ADHD provides alternative agents to consider when a patient fails to adequately respond or cannot tolerate traditional medications.

Abuse, Misuse and Diversion

Treatment of adolescent and adult ADHD has been approached by some clinicians with trepidation because of questions of diagnostic validity, very limited residency training and a discomfort with using stimulants in this patient population. In a survey of 400 primary care physicians (PCPs) who regularly treat mental health disorders, approximately half of the respondents reported that they were not confident diagnosing ADHD in adults and 44% considered the diagnostic criteria for adult ADHD to be unclear.[22] Approximately three-fourths believed it is more difficult to diagnose ADHD in adults than in children. Two-thirds of PCPs deferred to a specialist when diagnosing ADHD in adults, compared with 2% of PCPs for depression and 3% of PCPs for generalized anxiety disorder.

One issue that receives media attention is concerns about abuse, misuse and diversion of stimulant medications. Bright and colleagues[23] are conducting a large survey of substance-abusing patients (N=1000) to evaluate what drugs they seek and select for abuse. The interim report of 545 participants ages 12 and older (with 56% between ages 12 and 25) reveals 19.4% had abused stimulants by crushing/inhaling, crushing/injecting or melting/snorting. They were much more likely to abuse immediate-release stimulants than the extended-release formulations. Volkow and Swanson[24] have demonstrated that the abuse potential of the drug is related to the rate of rise in serum blood levels and the rate of dissociation from dopamine neuroreceptors. Therefore, it appears possible to reduce the likelihood of abuse and diversion by prescribing extended-release stimulant preparations.

ADHD Comorbidity

The National Comorbidity Survey Replication (NCSR) queried 9,282 adults of whom a subset of 3,199 made up the data for adult ADHD.[25] The study estimated the prevalence of adult ADHD at 4.4% in the general population. Patients present to clinicians with the most distressing or impairing symptoms. Anxiety and depressed mood are frequently the presenting complaints in a primary care or psychiatric office. Of adults with MDD, one in 10 have ADHD; of adults with BD, one in five have ADHD; for those with chronic dysthymia, more than one in five have ADHD; and of the adults with active substance abuse, more than one in 10 have ADHD. These findings highlighted that ADHD in adults needs to be assessed at the initial evaluation despite the presenting complaint.

Adults with ADHD often suffer with other psychiatric conditions.[25] The NCSR data demonstrated that 38.3% of adult patients with ADHD also have a mood disorder. Adults with ADHD may also have anxiety disorders at a rate of 47.1% with social anxiety disorder at 29.3%, posttraumatic stress disorder at 11.9%, panic disorder at 8.9%, generalized anxiety disorder at 8.0%, agoraphobia at 4.0% and OCD at 2.7%.

Although there has been a growing body of research in adult ADHD, and clinicians are increasingly aware of the disorder in adults, the treatment of adult patients with ADHD remains quite low at 10.9%.[25]

Treating Comorbidities

Since the clinical presentation of adult patients with

ADHD is concurrent with comorbid psychiatric conditions, it is important to understand how to diagnostically prioritize comorbid disorders in order to create a pharmacologic algorithm. There is developing research that may offer clinicians some guidance.

In the area of substance abuse disorder and adult ADHD, there are 13 studies that have looked at the treatment of ADHD. Ten of the 13 studies involved cocaine dependence. Most of the studies started with participants with untreated ADHD and untreated cocaine use. Seven of the 13 studies used methylphenidate to treat the ADHD and monitored effect on cocaine use. Levin and colleagues[26] conducted a 14-week, randomized, controlled trial using sustained-release methylphenidate to treat ADHD in 106 active cocaine-dependent treatment seekers. All participants received weekly individual cognitive-behavioral therapy (CBT). Using a combined outcome of >30% reduction in ADHD symptoms and Clinical Global Impressions (CGI) scale score <3, the response rates were similar and not significant (28% placebo versus 30% methylphenidate; P=0.83). Longitudinal urine toxicology indicated a significant reduction in cocaine use in the methylphenidate arm versus placebo. Treatment trials with bupropion, venlafaxine, bromocriptine (Parlodel), pemoline (Cylert) and psychotherapy also have been studied.

Published studies in adult ADHD with BD are scant. Only one published study exists: an open-label, six-week trial of bupropion sustained-release (up to 200 mg bid).[19] Participants (N=36; 90% with bipolar II disorder) who were stable on mood stabilizers and antipsychotics enrolled in the trial. Bupropion was associated with a significant reduction on the ADHD symptom checklist and improvement in CGI-severity (CGI-S) scale without activating mania.

The published studies on the treatment of adult ADHD in the presence of MDD are equally scant. In one retrospective analysis, 17 participants with MDD and ADHD received one of three treatments: venlafaxine, bupropion or tricyclic antidepressant monotherapy; stimulant monotherapy; or stimulant plus antidepressant therapy.[27] Patients on stimulants plus an antidepressant demonstrated a significant improvement in both MDD and ADHD symptoms versus stimulant monotherapy. The quality of the data make this a very preliminary finding. In an open-label trial of four adults whose depression was first treated with fluoxetine (Prozac) or sertraline (Zoloft) monotherapy followed by a stimulant for the treatment of ADHD, the combination treatment was found effective.[28]

With the preliminary research at this time, the recommended diagnostic prioritization calls for the treatment of active alcohol and substance abuse first, then severe mood disorders, followed by severe anxiety disorders and finally ADHD.[18] In diagnostically prioritizing the concurrent disorders, the most impairing disorder should be treated first. There are several reasons to structure the approach this way. First, the cognitive impairments seen in adult ADHD can be produced by other active psychiatric conditions. Second, the medications used to treat ADHD may make the untreated co-existing psychiatric conditions worse.

Table ***CYP450 Inhibitory Effects of ADHD Medications***

Medication	Cytochrome P450 Isoenzymes: 1A2	2C8	2C19	2D6	3A4
Amphetamine	0	0	0	[illegible]	0
Methylphenidate	0	0	0	0	0
Atomoxetine	0	0	0	[illegible]	0
Bupropion	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Desipramine	0	0	0	[illegible]	0

[illegible]

Polypharmacy

Given that pharmacologic treatment of concurrent active psychiatric disorders often requires polypharmacy, it is important to understand the possible clinically relevant kinetic drug-drug interactions. In the **Table**, the degree of cytochrome P450 enzyme inhibition is listed for the medications used in the treatment of ADHD. Notice that the stimulant medications have no inhibitory effects while atomoxetine and bupropion have significant 2D6 inhibition. This may be a consideration when substrates of 2D6 like risperidone (Risperdal), codeine or nortriptyline (Aventyl, Pamelor) are coprescribed with atomoxetine or bupropion.[29,30]

Cardiovascular Concerns

In the recent past, the FDA has required product label changes on stimulant medications to reflect cardiovascular and psychiatric safety concerns. These changes have required physicians to improve the ways they assess the cardiovascular risk of patients. The issue of sudden death is a safety concern in children and young adults. The specific cardiovascular structural and electrical abnormalities associated with this risk are congenital long QT interval syndrome, arrhythmogenic right ventricular dysplasia, aberrant coronary artery

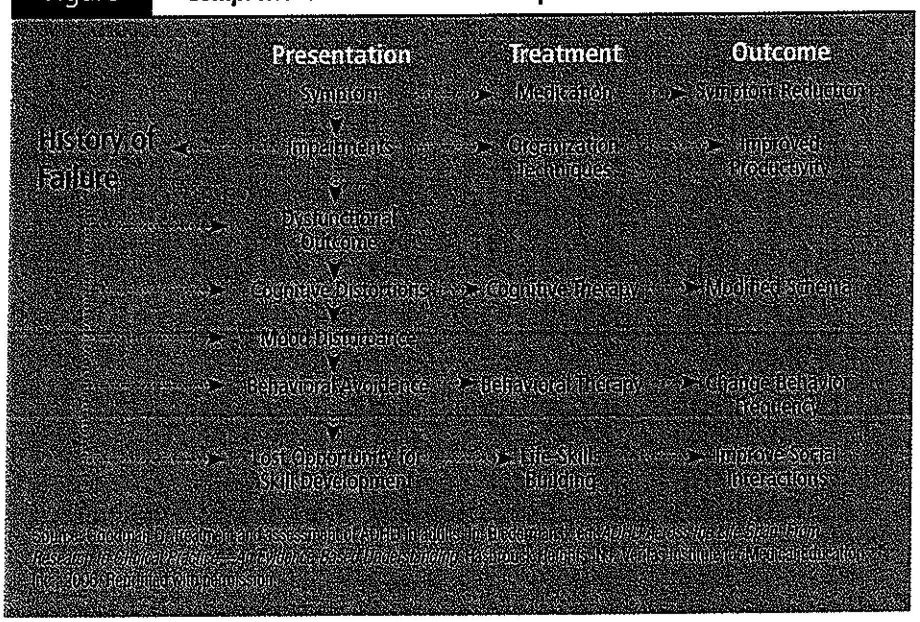
and hypertrophic cardiomyopathy.[31]

The former two are detectable on electrocardiogram or Holter monitoring; the latter two abnormalities are detectable on echocardiogram. All abnormalities are highly familial. Unfortunately, one cannot tell who is at risk by looking at the patient. Therefore, in order to judge potential risk, the presence of the following should be ascertained:

- Spontaneous syncope
- Exercised syncope and/or chest pain
- Sudden death in family member before age 30
- Family history of electrical or structural abnormalities

If any are present, then the decision whether to follow up with a cardiac evaluation before initiating stimulant medication needs to be made.[32]

Figure ***Comprehensive Role of the Therapist***



Pregnancy and Breast-Feeding

Pregnancy is an issue specific to and common in females with ADHD. They remain at higher risk for unplanned pregnancy than females without ADHD, especially when the ADHD is untreated.[33] It is important to remember that stimulant medications and atomoxetine remain category C medications and are not recommended during pregnancy and breast-feeding.[34] Studies have detected methylphenidate and dextroamphetamine in breast milk.[35-38]

Psychotherapy

Although medication is a cornerstone in the treatment of adult ADHD, individualized psychotherapy provides complementary benefits to patients and their families. There are several therapeutic approaches to consider, but to be most effective the key target symptoms and impairments need to be identified. The **Figure** provides an outline of specific target symptoms and the appropriate therapeutic approach.

Of the therapy approaches, CBT seems to have the best ability to introduce new cognitive skill sets. Preliminary evidence for CBT in adult ADHD is noted in open-label studies[39] and controlled trials.[40] Safren and colleagues[40] investigated CBT in a randomized, controlled trial of 31 adults with ADHD who were stable on medication and then randomized to medication and CBT or medication only. The CBT used in the study was conceptualized in three modules: 1) Organizational and planning skills; 2) Reducing distractibility; and 3) Cognitive restructuring. Several assessment scales, both investigator-rated (Hamilton Rating Scale for Depression [HAM-D], Hamilton Rating Scale for Anxiety [HAM-A] and CGI-Improvement [CGI-I]) and self-rated (Current Symptoms Scale [CSS], Beck Depression Inventory [BDI] and Beck Anxiety Inventory [BAI]), were used to evaluate outcomes. Mean ADHD scores declined 14.2 points for CBT plus medication ($P<0.01$) versus 5.2 points for the medication-only group. Improvement was noted on all assessment scales in the CBT plus medication group, and this group had more treatment responders versus medication alone (56% versus 13%).

A thoughtful conceptualization and application of psychotherapy will prevent the therapist from being distracted. Since it is the very nature of the patient to be disorganized and distractible, organization and focus on the part of the therapist is critical to ensure adherence to the therapeutic pursuit.

Although empirically tested research on psychotherapies in adult ADHD is very limited, these few studies do suggest that a specific mode of therapy could complement the benefits of medication.[39,40] Positive controlled trials of a specific therapeutic method would help standardize the psychotherapeutic approach for optimal treatment outcome for adults with ADHD.

In conclusion, the treatment of ADHD in adolescents

and adults has an increasing number of pharmacologic and psychotherapeutic options. Titration of medication should be based on symptom reduction, optimal daily functioning and tolerability. Symptom rating scales performed sequentially throughout treatment complement the clinical interview in dosing considerations. Concurrent psychiatric comorbidities need to be assessed at the inception of treatment so that a diagnostic prioritization can lead to a thoughtful pharmacologic algorithm. The resulting polypharmacy requires an understanding of the safety and tolerability issues that guide medication selection. Emerging research on psychotherapy supports its use to complement the medications, teach psychological skills and optimize treatment outcome.

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1. Which of the following challenges associated with diagnosing ADHD in adolescents and adults are inherent in the current *DSM-IV* criteria?
   a. Adults often have difficulty recalling and reliably or accurately describing symptoms and impairment in childhood.
   b. It is difficult to gather information from adolescents and adults about symptoms and impairments in multiple domains.
   c. Some of the *DSM-IV* symptoms of ADHD are developmentally inappropriate for adults.
   d. Many, if not most, adults with ADHD have comorbid conditions, making it difficult to determine the exact nature of the reported symptoms.
   e. All of the above.

2. Which of the following is most accurate regarding QoL measures in studies with ADHD patients?
   a. Studies of QoL in children, but not adults, with ADHD demonstrate significantly lower QoL compared to control children.
   b. Studies of QoL in adults, but not children, with ADHD demonstrate significantly lower QoL compared to control adults.
   c. Studies show that QoL for patients with ADHD is poor, but is still better than individuals with other chronic diseases, such as cancer and cerebral palsy.
   d. Treatment studies that have measured QoL in patients with ADHD have often shown a lack of correlation between changes in symptom scores and changes in QoL.
   e. None of the above.

3. Individuals with ADHD are at increased risk for which of the following?
   a. Non-nicotine SUDs
   b. Nicotine and non-nicotine SUDs
   c. Driving problems
   d. a and c
   e. All of the above

4. For an adult patient with ADHD only, which treatment option is likely to yield the best outcome?
   a. Medication alone
   b. Cognitive-behavior therapy alone
   c. Combination of family therapy and behavioral techniques
   d. Combination of focused psychotherapy and medication

5. There is a substantial amount of research that establishes how to treat comorbid psychiatric disorders in the presence of adult ADHD.
   a. True
   b. False

6. Knowing which of the following will NOT help in assessing cardiovascular risk for sudden death?
   a. Exercise-induced chest pain or dizziness
   b. Sudden death in family member before age 30
   c. Positional dizziness
   d. Spontaneous syncope

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