

M E D I C A L

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SPECIAL EDITION

Identification and Discussion of Key Issues and Advances in Pediatric ADHD

CME-Certified Activity

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Educational Overview

Attention deficit hyperactivity disorder (ADHD)—the most commonly diagnosed and treated behavioral disorder of childhood—is associated with significant morbidity in the realms of social and academic success, and self-esteem. It is therefore essential that clinicians be knowledgeable about the presentation and diagnosis of ADHD so that individuals with this disorder receive appropriate treatment. At the same time, developing a treatment plan for individual patients that optimizes the use of available pharmacological and non-pharmacological strategies represents an important clinical challenge for those managing these patients.

This *Medical Crossfire* activity, conducted in conjunction with UMDNJ, will discuss these and other issues related to treatment options and advances for treating pediatric ADHD.

Target Audience

This educational activity is designed for psychiatrists, pediatricians, primary-care physicians, and other healthcare professionals interested in or involved with the management of ADHD in pediatric populations.

Learning Objectives

- Review important aspects of the clinical picture of pediatric ADHD in patients at various stages of development
- Describe the role of multimodal strategies of treating pediatric patients with ADHD.
- Discuss strategies for optimizing the use of currently available therapies in the management of pediatric ADHD.
- Consider the potential impact that advances in therapeutic strategies may have on clinicians' ability to individualize treatment.

Method of Instruction

Participants should read the learning objectives and review either the monograph or the audio CD in its entirety. After reviewing the material, complete the self-assessment test consisting of a series of multiple-choice questions. The activity is complemented with references that contain the rationale for the correct answer to each question, allowing participants to review the material as needed, thus finalizing their educational participation.

Upon completing this activity as designed, participants will receive a letter of credit awarding AMA/PRA category 1 credit three to four weeks after receipt of the registration and evaluation materials. Estimated time to complete this activity as designed is one (1) hour.

Accreditation

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of UMDNJ—Center for Continuing and Outreach Education and *Medical Crossfire*/Liberty Communications Network. UMDNJ—Center for Continuing and Outreach Education is accredited by the ACCME to provide continuing medical education for physicians.

UMDNJ—Center for Continuing and Outreach Education designates this educational activity for a maximum of one (1) category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity.

The print monograph was reviewed for relevance, accuracy of content, balance of presentation, and time required for participation by Sherie Lynn Novotny, MD; Syed Hasan, MD; Mark Miceli, MD; and Elena Volfson-Doubova, MD. The audio CD was reviewed by Sherie Lynn Novotny, MD; Richard Brodsky, MD; John F. Schiltz, MD, PhD; and Mohammad Siddiqui, MD.

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Disclosure Declarations

In accordance with the disclosure policies of UMDNJ and to conform with ACCME and FDA guidelines, all program faculty are required to disclose to the activity participants: 1) the existence of any financial interest or other relationships with the manufacturers of any commercial products/devices, or providers of commercial services, that relate to the content of their presentation/material, or the commercial contributors of this activity, that could be perceived as a real or apparent conflict of interest; and 2) the identification of a commercial product/device that is unlabeled for use or an investigational use of a product/device not yet approved.

Faculty Disclosure Declarations

Dr. Findling has received grant/research support from Abbott Laboratories, AstraZeneca Pharmaceuticals, Bristol-Myers Squibb, Celltech-Medeva, Eli Lilly & Co., Forest Laboratories, GlaxoSmithKline Pharmaceuticals, Johnson & Johnson, New River Pharmaceuticals, Novartis Pharmaceuticals Corp., Otsuka America Pharmaceutical, Pfizer Labs, Shire US, Inc., Solvay Pharmaceuticals, and Wyeth Pharmaceuticals; has been a consultant for Abbott Laboratories, AstraZeneca Pharmaceuticals, Bristol-Myers Squibb, Celltech-Medeva, Eli Lilly & Co., Forest Laboratories, GlaxoSmithKline Pharmaceuticals, Johnson & Johnson, New River Pharmaceuticals, Novartis Pharmaceuticals Corp., Otsuka America Pharmaceutical, Pfizer Labs, Sanofi-Synthelabo Pharmaceuticals, Shire US, Inc., Solvay Pharmaceuticals, and Wyeth Pharmaceuticals; has served on the speakers' bureau of Shire US, Inc; and has been a member of the scientific advisory boards of Abbott Laboratories, AstraZeneca Pharmaceuticals, Bristol-Myers Squibb, Eli Lilly & Co., Forest Laboratories, GlaxoSmithKline Pharmaceuticals, Johnson & Johnson, New River Pharmaceuticals, Novartis Pharmaceuticals Corp., Otsuka America Pharmaceutical, Pfizer Labs, Shire US, Inc., Solvay Pharmaceuticals, and Wyeth Pharmaceuticals.

Dr. Manos has received grant/research support from McNeil Consumer and Specialty Pharmaceuticals, Noven Pharmaceuticals, and Shire US, Inc; has been a consultant for Eli Lilly & Co., McNeil Consumer and Specialty Pharmaceuticals, and Shire US, Inc.; and has served on the speakers' bureaus of Eli Lilly & Co., McNeil Consumer and Specialty Pharmaceuticals, and Shire US, Inc.

Dr. Salgo has no financial arrangements or affiliations to disclose.

Dr. Wilens has received grant/research support from, has been a consultant for, and has served on the speakers' bureaus of Abbott Laboratories, Alza/Ortho-McNeil Pharmaceuticals, Cephalon, GlaxoSmithKline Pharmaceuticals, Janssen Pharmaceutica Products, Eli Lilly & Co., NIDA, NIMH, NICMH, Neurosearch, Novartis Pharmaceuticals Corp., Pfizer Labs, Saegis, Sanofi-Synthelabo, and Shire US, Inc.

Dr. Novotny has received grant/research support from Bristol-Myers Squibb; and has been a consultant for Shire US, Inc.

Dr. Brodsky, Dr. Hasan, Dr. Miceli, Dr. Schiltz, Dr. Siddiqui, and Dr. Volfson-Doubova have no financial arrangements or affiliations to disclose.

Off-Label Usage Disclosure

This program contains discussion of commercial products/devices that are unlabeled for use or investigational uses of products not yet approved. Tricyclic antidepressants, the novel antidepressant bupropion, selective serotonin reuptake inhibitors, alpha-andrenergic agents, and monoamine oxidase inhibitors are not indicated for the treatment of ADHD in adults or children. An application for approval of the methylphenidate transdermal system (MTS) has been submitted to the US FDA and is currently under review.

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Identification and Discussion of Key Issues and Advances in Pediatric ADHD

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Attention-deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed and treated psychiatric disorder of childhood, affecting approximately 5% of the population.¹ This serious neurophysiologic disorder is associated with problems of self-esteem as well as significant morbidity in the realms of social and academic success.² Appropriate treatment however, has been demonstrated to provide rewarding and long-term benefits for both children with ADHD and their families. It is therefore essential for clinicians to be knowledgeable about the presentation and diagnosis of ADHD, and to be confident in choosing among available and emerging therapeutic options. To assist clinicians in understanding current issues and advances in pediatric ADHD, *Medical Crossfire* convened a panel of experts to offer their insights on the optimal treatment of this disorder.

Current Perspectives

ADHD, a psychiatric disorder defined as a persistent pattern of inattention and/or an inability to control behavior that is more severe than typical for a child's developmental level, is present in approximately 2 million American children. In any classroom of 25 to 30 children across the United States, it is likely that at least one student will have ADHD.³ To begin the *Medical Crossfire*, moderator Peter L. Salgo, MD, asked, "Why is it important to diagnose and treat ADHD in the pediatric patient?"

The Burden of ADHD

"ADHD is a disorder that carries with it substantial impairment that often continues throughout the patient's life," answered Timothy E. Wilens, MD. Once thought to remit before or during adolescence, ADHD is now estimated to continue into adolescence in more than three quarters of cases and into adulthood in up to 65% of cases.⁴ "If you do not identify and treat this disorder," cautioned Dr. Wilens, "the significant problems and sequelae of ADHD—starting with acad-

emic underachievement and extending to a whole host of major problems, including morbidity and mortality—will begin. And if you intend to treat ADHD, you must start with a solid and systematic diagnosis."

"What are some specific quality-of-life issues that are associated with the pediatric ADHD patient?" inquired Dr. Salgo.

"A number of studies have demonstrated that these individuals have significantly more difficulty with academic achievement and academic performance,^{5,6}" noted Dr. Wilens, adding that lower academic achievement "is an independent risk factor for not doing well in life such as substance abuse, occupational underachievement, and criminality."

Among the other negative outcomes associated with untreated ADHD, continued Dr. Wilens, are "low self-esteem, difficulty with peer interactions, and increased risk of injuries, motor vehicle accidents, cigarette smoking, and substance-abuse disorders.⁶⁻¹² As pediatric patients become adults, this list goes on to include occupational underachievement and more legal involvement.⁷ This is just a partial list of the impairments associated with ADHD across the lifespan."

ADHD: Why Controversy Persists

“The list of negative outcomes associated with the disorder is very substantial, and makes it sound as if ADHD really needs immediate therapy,” commented Dr. Salgo. “So the next obvious question seems, Should people still be debating the existence of ADHD?”

“A debate about whether or not ADHD is a real disorder is an unfortunate debate,” asserted Michael J. Manos, PhD. “It is fueled, it seems, by people who are not well informed. But there is no question about the biogenetic basis of ADHD. There is no question about the impact of the disorder on the quality of a patient’s life.”^{13, 14}

“Why are people still debating this diagnosis?” pursued Dr. Salgo.

“That is a very good question,” ventured Robert L. Findling, MD. “I cannot give you a reason why the debate occurs, but I can tell you that for a long time people did not acknowledge ADHD, and subsequently people behaved as if it were not there. Now we understand that it is there, that it can be treated, and that treatment can make a difference in patients’ lives.”

“One issue that perpetuates this debate is that the symptoms of ADHD also appear in normal people in everyday life,” posited Dr. Wilens. “Children without ADHD may have transient problems with academics, and with attention or focus. Most children manifest hyperactivity at some point in their life—these are ‘everyday dysfunctions’ that do not necessarily mean that a child has ADHD. So a person might reason, ‘my child or I have these nonspecific symptoms and we do not have ADHD, so I will assume that most people with ADHD really do not have the disorder, either.’”

“Yes, these are common symptoms, but isn’t that true of most psychiatric illnesses, except the most extreme?” queried Dr. Salgo. He proposed that the difference between normal symptoms and clinically diagnostic symptoms is a matter of degree.

“At the end of the day, it is not just the degree, but also the associated dysfunction,” replied Dr. Findling. Using visual impairment

as a metaphor, he explained, “People who are nearsighted can see, but everything is blurry; nearsightedness is an accentuation or distortion of normal vision. In many ways, ADHD is really not just an accentuation of something that happens normally. If the eyes do not focus well we call it nearsightedness; if the mind does not focus well because of a neurobiological dysfunction we call it ADHD. Part of the confusion arises from the fact that there is no ‘objective’ measure of ADHD.”

Recognizing and Diagnosing ADHD

The diagnosis of ADHD can be a complicated and challenging process, as the disorder manifests differently at various stages of human development. In addition, its key features— inattention and hyperactivity/impulsivity— are symptoms of many other disorders. Furthermore, approximately 65% of children with ADHD have at least one other comorbid condition, including depression, conduct disorder, oppositional defiant disorder, Tourette’s syndrome, and learning disabilities, among others.^{15, 16} The clinician’s role is further complicated by the absence of laboratory tests and imaging studies that can detect ADHD. “But there are clinical criteria for making the diagnosis,” remarked Dr. Salgo, who then asked Dr. Findling to review them.

“The current criteria focus on two symptom clusters: one of inattention, and one of hyperactivity and impulsivity,” responded Dr. Findling, adding that “patients must have substantial dysfunction in one of these domains” to qualify for a diagnosis of ADHD. According to the most recent version of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR), three subtypes of ADHD are recognized by professionals: predominantly hyperactive-impulsive type, predominantly inattentive type, and combined type.¹⁷ “It is not just the symptom clusters that characterize this condition,” pointed out Dr. Findling, “but also the fact that it is a chronic disorder characterized by the diver-

gance from expected development in certain domains of functioning.”

“And what does the DSM-IV-TR say about these patterns of behavior that can really help to pinpoint the diagnosis of ADHD?” inquired Dr. Salgo.

“I do not think anything actually nails the diagnosis, and that is probably where part of the controversy about the validity of ADHD comes from,” replied Dr. Findling. “What really characterizes a youngster with ADHD is the longitudinal course of chronic dysfunction in the absence of other explanations for the problems. So it is not simply the symptoms that indicate ADHD but the overall clinical picture and longitudinal course.”

When Is It ADHD?

Reminding participants that making an accurate diagnosis of ADHD requires consideration of the type of behavior that is typical for a child’s developmental level, Dr. Salgo asked, “How does the clinical picture of, for example, a preschooler with ADHD differ from that of an adolescent with ADHD? When is it ADHD and when is it just a normal stage of development?”

“That is a terrific issue,” commented Dr. Wilens, positing that there are two overriding considerations in understanding the changes in the presentation of ADHD across the lifespan. “One is natural change in the symptoms over time. The other is the introduction of new and challenging tasks at various stages of development that may challenge different aspects of the child and bring out vulnerabilities. “Let me start with the former: natural change in symptoms,” continued Dr. Wilens. “Children who do not have ADHD have some hyperactivity and impulsivity when they are younger and tend to lose the hyperactivity and impulsivity over time. Children with ADHD, however, demonstrate the same phenomena but they start at much, much higher levels of both hyperactivity and impulsivity than their peers. Over time, the levels of hyperactivity

and impulsivity may become normal or may continue to be problematic, but generally there will be a relative diminution of the hyperactivity and the impulsivity.

“What tends not to get better,” he went on, “is the attentional cluster of symptoms: inattention, lack of concentration, forgetfulness, shifting activities, executive operation dysfunction and disorganization. These symptoms tend to persist in children with ADHD, even as they grow older and the tasks expected of them increase. Preschoolers tend not to have as many cognitive challenges; therefore, these children seem to have more impulsivity and hyperactivity. As they age and are given more cognitive tasks, they begin to demonstrate more of the attentional dysfunction. In the first, second, and third grades, children are expected to sit in their seats for an extended period and to apply themselves to learning. As these cognitive tasks begin to challenge the child there is a greater manifestation of symptoms such as inattention and disorganization.”

Dr. Salgo inquired, “What are some specific challenges associated with managing ADHD of the predominantly inattentive type?”

“Oftentimes, the problem that is identified in youngsters with ADHD is not underachievement but disruptive behavior,” replied Dr. Findling. Therefore, he noted, the youngster who is performing quietly but poorly in school or the youngster who is underachieving may not be recognized as having ADHD.

Adults, noted Dr. Findling, “may not pay attention to these children, or they may label them as lazy and assume that they are really not trying hard enough. And so the issues with inattention, although different than the issues with hyperactivity and impulsivity, are just as impairing, just as debilitating, and associated with the same kind of distress and human suffering as a youngster who is getting into trouble for disruptive behavior.”

“What are the diagnostic challenges in diagnosing a patient with the inattentive type

of ADHD, and how can they be overcome?" asked Dr. Salgo.

Dr. Manos emphasized the importance of "taking a careful look at the broad spectrum of behavior and compiling good, solid information from several different sources." Providing an illustrative example, Dr. Manos proposed, "a child may be doing very well in school, but the amount of time and energy that a parent expends helping the child with her homework at the end of every day goes unrecognized. Often, there is a level of involvement and engagement by the parent in which the adult rather than the child is actually performing the required executive function of the brain. When the parent performs the brain's executive function for the child, that is a dysfunction."

Another tactic, offered Dr. Manos, is to look into a child's level of social engagement. A child with one friend but no other social outlets, for example, may require close investigation. To summarize, Dr. Manos suggested that clinicians "tap into a broad spectrum of symptoms that are expressed in a child's life."

Gender Issues in ADHD

Focusing on the issue of inattention as opposed to hyperactivity/impulsivity, Dr. Salgo noted that girls have been found to more often display the inattentive type of ADHD.¹⁸ "What is the role of gender in ADHD?" he asked. "Are there differences in presentation and diagnosis?"

"There is a tendency for boys to be diagnosed earlier than girls, and there is also a higher ratio of boys to girls receiving a diagnosis of ADHD in childhood," answered Dr. Manos. In clinic-referred samples of school-age children, the ratio of boys to girls with ADHD ranges from 3:1 to 9:1, whereas, in community-based samples, the ratio is 2:1.¹⁹ Dr. Manos posited that the gender-based diagnostic differences might be explained, in part, by the fact that "boys are represented by more hyperactivity and subsequently are

noticed more readily. Girls tend to have ADHD problems show up at a later time because inattention is not readily noticeable at very young ages.

"One of the most telling factors is the gender difference in changes in locus of control," he continued, citing a study by Rucklidge and Tannock.²⁰ These authors found that girls with ADHD aged 13 to 16 were at higher risk for several types of psychological impairment as compared with both same-age boys with ADHD and normal girls. One of the impairments more common in girls with ADHD was a diminished locus of control. "Girls, in general, lose a sense of inner locus of control—that is, a sense that they control their lives and control the circumstances of their lives," explained Dr. Manos. This loss occurs more frequently and at an earlier age in girls with ADHD as compared with both boys with ADHD and normal girls, he added. "A sample patient in this case would be a young girl who is very bright, but who sits in the back of the classroom and gets Cs on her report card. She does not feel that she controls the factors and circumstances in her life.

"There are also differences between boys and girls in social relationships and maintaining social relationships," continued Dr. Manos, "Girls in a summer camp were able to make friends but were unable to keep them."^{21,22} Boys tend to have difficulty both making and keeping friends."²³

"Clinicians must realize that there are many more similarities than dissimilarities between the sexes when it comes to ADHD," cautioned Dr. Wilens, pointing to the work of Hinshaw and colleagues, who have published a series of papers on the largest sample of girls with ADHD,²⁴⁻²⁶ and that of his own team, which has performed a controlled family study of girls with ADHD.²⁷

"There is a great deal of anecdotal information saying that girls are different than boys," continued Dr. Wilens, but the research literature reveals that "girls have similar amounts of hyperactivity, impulsivity,

and inattention as boys as well as similar rates of co-occurring psychiatric problems. Girls tend to have less conduct disorder and less oppositional disorder than boys, whereas they have the same rates of other disorders. Girls and boys have the same rates of depression, anxiety, and learning disabilities.”

Dr. Wilens suggested, however, that there is “a bit of a bias against the girls” in terms of recognition and diagnosis. “Survey studies indicate that teachers are more familiar with boys with ADHD than girls with ADHD. This is of concern in that, when you look, you will see ADHD in girls and if you do not think to look, you will miss it.”

“The point Dr. Manos made about girls’ sense that they have lost their locus of control is a very cogent one and dovetails with a recent survey study by Quinn and Wigal,” continued Dr. Wilens. In this study based on an interactive online interview, perceptions of girls with ADHD were elicited from members of the general public, teachers, parents of children with ADHD, and children with ADHD.²⁸ “When boys with ADHD and girls with ADHD were asked about themselves,” reviewed Dr. Wilens, “one of the striking differences is that girls talked about how much they suffered with the condition, diagnosed or undiagnosed. They felt internally stigmatized.” In addition, he noted, girls were more likely than boys to report negative self-esteem, prior antidepressant treatment, problems focusing on schoolwork, and difficulty getting along with parents. Concluding his comments, Dr. Wilens suggested, “We need to focus attention on girls and realize that girls as well as boys have the disorder.”

Insights into Diagnosis

Clinicians must employ a combination of techniques—including clinical interviews, assessment instruments, and physical examination—to arrive at a diagnosis of ADHD, to rule out any conditions that may masquerade as ADHD, and to identify comorbid conditions. Dr. Salgo asked, “What tools can be used to make a diagnosis of ADHD?”

“There are a number of different tools that can be used, and one of the most common is a rating scale,” answered Dr. Manos, who cautioned that “a diagnosis should never be based on a rating scale alone but should utilize data from rating scales to complement other information.”

Typically used are broadband rating scales such as the Child Behavior Checklist (CBCL) or the Behavior Assessment System for Children (BASC), which can help to distinguish ADHD from other psychiatric diagnoses and screen for comorbidities, continued Dr. Manos. If the broadband rating scale suggests ADHD, he advised using “a narrowband rating scale that actually taps into the symptoms of ADHD as an accompaniment to the broadband rating scales, which reflect the norm across all ages. Rating scales can help one tap into symptoms, but accompanying the rating scales must be a good, solid Mental Status Exam [MSE] and an interview to identify the true presence and expression of these symptoms in a patient’s life.”

“The clinician really has to engage the adolescent in the discussion when the inattentive type is presenting,” agreed Dr. Wilens, noting that the inattentive type of ADHD is often identified at an age of approximately 15 years. In younger children, adequate information can be elicited from the parent, stated Dr. Wilens, “but, in ADHD diagnosed during adolescence, do not forget the adolescent in that process.”

“A key point is having multiple sources of information,” emphasized Dr. Manos.

Dr. Findling agreed with his colleagues and added, “The other key feature, of course, is the longitudinal course. It is not as if a teenager one day will wake up with ADHD.” In considering a diagnosis of ADHD, the clinician must also be aware that “there are many neuropsychiatric conditions other than ADHD that are associated with poor attention, academic dysfunction, and defiant-like behavior. These include depression and other mood disorders, anxiety disorders, and sometimes even psychotic illnesses.”

Dr. Wilens added psychosocial chaos, which may result from a traumatizing home environment, to the list of alternative diagnoses that must be considered. He then introduced a new topic. “I would also like to comment on the fact that pediatricians may be caught off-guard with inattentive ADHD in an adolescent patient,” he noted. “The pediatrician might think, ‘I have been following this child since she was two years old, and I have never heard any ADHD concerns. Now, at age 15, both parent and child are talking to me about ADHD. How can I have missed this diagnosis for 13 years?’”

This situation is a particular concern, he said, because most adolescents with undiagnosed inattentive-type ADHD present to pediatricians, according to research by Wolraich and associates, as well as other teams.²⁹ “These authors have shown that most inattentive-type ADHD patients are going to pediatricians and those with the combined subtype of ADHD are being seen by child psychiatrists, pediatric neurologists, and other clinicians who see ADHD frequently,” stated Dr. Wilens. Pediatricians and primary-care physicians may not have specialized knowledge of the longitudinal course and age-specific presentation of ADHD, he suggested.

“What is the answer to that question? How is it possible that ADHD has been missed?” inquired Dr. Salgo. “Is it a diagnosis that doctors need to be attuned to earlier?”

Referencing Dr. Wilens’ earlier comments, Dr. Manos pointed out, “There is an interaction between ADHD symptoms and the level of demand that is required of a child in any particular environment. Furthermore, there are several different transition points in which symptoms typically show up.”

Dr. Manos then reviewed these transitions as they occur throughout a child’s development to adulthood. “The first is kindergarten to first grade. First grade requires more sitting and more stationary activity. The second is fourth grade, where kids stop learning to read and start reading

to learn. In fourth grade, projects are bigger, and reports have multiple steps. The next transitions are obvious ones: first, the transition to middle school, when there are multiple classes; and, second, to high school, where classes are harder. In addition, there are two more transitions, the one to college and the one to the world of work, which requires self-generated organization and places increased demands on a person. Finally, there is one more transition, and that is when a person starts a family. The demands placed on an individual as a result of having a family multiply suddenly and incredibly, and people with ADHD are often not successful in managing those demands.”

“This brings up another question: Can a person outgrow ADHD?” asked Dr. Salgo. “Will that patient as an adult continue with ADHD through college, the workforce, and parenthood?”

Dr. Manos offered a brief anecdote in response. “A 79-year-old woman was recently brought into our adult clinic by her daughter, who claimed that the mother had been burdening the family for decades because of her ADHD. And, sure enough, the mother very clearly met symptom criteria for ADHD and symptoms could not be accounted for by other conditions.”

“The real question is, Can ADHD be diagnosed any time in the life span?” proposed Dr. Findling. The answer, he suggested, is that ADHD may be present whenever the affected person cannot meet developmentally appropriate demands placed on him. “A perfect example is the inattentive youngster who is doing well at school because his parents are spending an inordinate amount of time supporting and structuring the child; if that structure is removed, the child with ADHD may have their functioning fall.”

Strategies for the Successful Management of ADHD

The management of ADHD must be based on an individualized approach that addresses

the impairments specific to each patient. A number of psychotherapeutic and pharmacological interventions are available for use alone or in combination, allowing appropriate therapy to be tailored to the needs of the individual. Psychostimulants have long been the cornerstone of therapy for ADHD for their ability to reduce hyperactivity and impulsivity; improve the ability to focus, work, and learn; and potentially improve the physical coordination needed for tasks like handwriting and athletics.³ Multimodal therapies utilizing pharmacotherapy in conjunction with different kinds of psychotherapy are also receiving focused attention and study.

Current Issues in Psychotherapy

Noting that there are many specific types of psychotherapy, including cognitive-behavioral therapy (CBT), ADHD counseling, behavioral modification, parent training, and academic skills therapy, among others, Dr. Salgo asked, “What role do these therapies have? What types work best in which patients?” Because of the recent attention it has received in the literature, Dr. Salgo asked Dr. Manos to start the discussion by addressing the role of CBT in treatment.

“Cognitive-behavioral therapy does not have strong evidence in support of treating symptoms of ADHD at all,” answered Dr. Manos, contrasting this situation with the evidence that cognitive-behavior therapy is very effective for comorbid disorders such as depression, anxiety, and adjustment disorders.

“The treatment of the symptoms of ADHD in pediatric populations is at the point of contact—home and school,” he noted. “A combined approach of medicine and behavioral therapy should be used in the particular settings in which the behavior problems present themselves. By contrast, in adolescence and adulthood, when patients are confronting issues such as self-efficacy, ineffectual management of the environment or the vicissitudes of life, then cognitive-behavioral therapy can be effective. However,

CBT is not a treatment that has wide application for treating symptoms of ADHD in children.^{30,31}

“Cognitive-behavioral therapy is not the only kind of psychotherapy for children,” pointed out Dr. Manos. “Behavioral therapy can be effective, and systematic social skills training can certainly teach skills.³²⁻³⁴ But one of the most fundamental problems in behavioral therapy is the issue of generalization. Just as with medicine, when behavioral therapy is stopped the effects are no longer there.” One reason that behavioral therapy may be discontinued, he noted, is the financial burden. Citing a recent paper by Johnson and Abercoff, Dr. Manos stated, “In some cases, the cost-effectiveness of behavioral therapy over pharmacological therapy can be preclusive.”

According to Dr. Manos, behavioral therapy need not be reserved for the child alone. Parent training can provide the specialized skills and knowledge necessary to assist in managing the behavior of children with ADHD.⁵ Parents learn, for example, how to establish clear and effective communication, specific expectations for desired behaviors, and specific consequences when desired behaviors are not achieved. Dr. Manos commented, “There is a world of literature recently published indicating that when parents are trained in the use of household behavioral skills, they gain a sense of self-efficacy. They reduce stress in the household, and this, in and of itself, is therapeutic for the child, even though it is working indirectly with the child through the parent.”

A recent paper reported on parent training using a variety of methods and strategies, including in combination with pharmacological therapy,³⁵ continued Dr. Manos. “Parent training clearly made a significant difference in reports of the child’s behavior at home, although it did not significantly impact reports of child behavior at school.”³⁶

“Behavioral intervention in a summer treatment program is very effective when the program is, in effect evaporating,” observed

Dr. Manos. “And ongoing booster sessions in which parents learn to use language to modulate behavior can make a big difference. I want to make the point that behavior modification is not really about changing behavior in children. That happens secondarily. It is about changing behavior in the change agents around the child, which largely means parents and teachers. From this, in turn, child behavior changes.”

“So you are talking about changing the milieu in which the child operates in order to make the child operate better despite ADHD?” suggested Dr. Salgo.

“Well said,” confirmed Dr. Manos, who then provided several specific recommendations. “For parent training, Thomas W. Phelan’s *1-2-3 Magic: Effective Discipline for Children 2-12* is excellent, and Ross W. Greene’s *The Explosive Child* has also been demonstrated to be effective. They are easy to use and are manageable. In addition, there is a world of research consisting of single-subject studies showing that modification of the environment around the child—through techniques, for example, like contingency reinforcement—is effective.”

Contingency reinforcement, he explained, rewards desirable behavior and discourages unwanted behavior through access to certain privileges—for example, television and computer time. Dr. Manos continued, “It is important to note that in studies conducted in the 1970s and 1980s, Madsen and coworkers demonstrated that a ratio of four positive verbalizations to one negative verbalization is effective in managing children’s behavior in the classroom.”³⁷

“One very important point is that you cannot not use some form of punishment,” asserted Dr. Manos. Appropriate punishment, that is, evidence-based aversive consequences, include timeout, in which the child is removed from the scene of the unwanted behavior for a designated time; response cost, in which something of value is taken away from the child; and overcorrection, in which a child is required to repeatedly en-

gage in a corrective action for an infraction (e.g., a child may slam a door frequently so the parent requires the child to go through the door repeatedly in quick succession and close it quietly each time). Overcorrection teaches new behavior, corrects the intrusive behavior, and may allow the child to consider the consequences prior to acting. An aversive consequence that is usually not effective is spanking. Concluded Dr. Manos, “Punishment is useful when it is used appropriately to apply an aversive consequence that is likely to reduce the frequency of a behavior or the probability of it re-occurring. Both positive reinforcement and aversive consequences must be used for successful management.”

“Am I incorrect to assume that one way to measure the effectiveness of these interventions is to look at reductions in the children’s psychostimulant dose?” queried Dr. Salgo.

“A very good question,” remarked Dr. Manos. “In Pelham’s summer treatment program, he demonstrated that dosage can be reduced with a very intensive behavioral program.” The summer treatment program devised by William E. Pelham, PhD, was a major component of the Multimodal Treatment Study of Children with Attention-Deficit/Hyperactivity Disorder (MTA), the most intensive study ever undertaken for treatment of ADHD.³⁸ The MTA study evaluated 579 elementary school boys and girls (ages 7 to 9.9 years) with ADHD who were randomly assigned to one of four 14-month treatment programs: medication alone; behavioral treatment alone; a combination of both medication and behavioral treatment; and routine community care. The authors concluded first that medication management alone was superior to both behavioral treatment alone and routine community care; and, second, that combined treatment did not yield significantly greater benefit than medication management for core ADHD symptoms, although it did show modest advantages in non-ADHD symptoms and positive functioning outcomes.

In addition, the combined treatment program was associated with significantly lower medication doses than those used in the medication-alone program. Dr. Manos pointed out, however, that the behavioral treatment used in the MTA study was particularly intense, consisting of parent training, child-focused treatment, and a school-based intervention. Furthermore, the child-focused treatment—developed by Dr. Pelham—was an eight-week, full-day therapeutic summer camp comprising intensive behavioral interventions and academic skills reinforcement. “Most of the time, one is not able to use as intensive a behavioral program as Dr. Pelham’s summer treatment program,” noted Dr. Manos. “Can you reduce dosage with a very good behavioral program? Yes. Is the availability of a very intensive behavioral program such that one can reliably implement it? Many times, not.”

“At the end of the day, however, the clinical implications of ‘getting away with’ a slightly lower dose of medicine may not be quite that important,” suggested Dr. Findling. “Although we always want to be sure not to overmedicate, we also do not want to mislead people into thinking that youngsters are in harm’s way if they do not receive a lower dose of medicine.” Dr. Findling expressed concern that using lowered medicine doses as a gauge of the effectiveness of a behavioral intervention “implies that a slightly higher dose of medicine is somehow a bad thing.”

“Again, let me ask, can behavioral management be deemed effective if the child must continue to take the same dose of medication?” pursued Dr. Salgo.

“It is effective if it helps the well-being of the youngster,” asserted Dr. Findling. Returning to the metaphor of near-sightedness, he proposed a classroom with a bigger blackboard, large-print books, and fewer pupils to allow children to sit closer to the teacher. “In this classroom, the nearsighted child might be able to get away with less correction in her glasses, but that does not mean those glasses will function adequately in the rest of

the world,” he explained. “Likewise, these day-treatment programs provide a structure that makes it easier for children with ADHD to ‘see.’ Ultimately, the goal is to help the child to learn. We should focus on finding the means to achieve that goal and not on whether the dose of medicine is as low as possible or whether a nonpharmacological intervention is consistent with some school of thought.”

Current Issues in Pharmacotherapy

Stimulant medications are available in short- and long-acting formulations and have been successfully used to treat ADHD since the 1930s.³⁹ According to one report by the American Medical Association,⁴⁰ as many as 90% of children with ADHD will respond to at least one appropriately dose-titrated stimulant without experiencing a major adverse event, although this percentage may be lower in those with comorbidities. For those patients who are not responsive or are unable to tolerate stimulant medications, several nonstimulant agents are available. To begin the discussion of current issues in the pharmacological treatment of ADHD, Dr. Salgo asked, “Are there any children who should be treated with medication alone?”

“There are certainly youngsters who may benefit from medicine alone, especially those who are under the care of a good pediatrician in a supportive home environment as well as those who are under the care of a good mental-health provider who is able to carefully monitor the youngster’s well-being,” answered Dr. Findling.

“To simply take a broad-brush stroke and say that everybody with ADHD needs one thing really does not serve the interests of the individual,” maintained Dr. Findling. “If a youngster is being treated with medicine as monotherapy and is doing well, is able to do all the things a child should do, then this youngster may not necessarily require any other form of intervention. The notion, I believe, should be to meet the child

where he lives. Give the help that is necessary and not the help that might not be necessary.”

“No child is ever treated with medicine alone; there are always people around a child doing something that has an effect on that child,” posited Dr. Manos. “The point that Dr. Findling makes about the influence of teachers, parents, and other caregivers is an excellent one. A family that is caring and nurturing and provides a consistent, predictable home environment to the child with ADHD—is providing effective behavioral intervention.”

Safety of Stimulant Medications. Although some parents express concern that stimulants may cause drug abuse or dependence, a review by Dr. Wilens’ team of all long-term studies of stimulants and substance abuse showed that drug abuse was less likely in children with ADHD who were treated with stimulants as compared with those who were not.⁴¹ “Should clinicians be concerned about the safety of these psychostimulant agents in pediatric patients?” asked Dr. Salgo.

“As both Dr. Manos and Dr. Wilens have alluded to earlier in this *Medical Crossfire*, ADHD is not a benign condition to be trivialized,” declared Dr. Findling. “This is a condition associated with real morbidity, profound human suffering, and the potential for mortality. ADHD is a big deal.”

Placed within the context of the serious nature of the disorder, he continued, the question can then be addressed. “Of course we are concerned about the pharmacological treatment of these youngsters, because no medicine is perfect. But studies show that treatment with psychostimulant medication provides benefits that fall within the risk-benefit ratio of concerns about the medicine versus the prognosis of the condition.”^{5,40,42-44}

“What are the indications and contraindications for stimulant use?” asked Dr. Salgo.

“The contraindications for psychostimulants include glaucoma, hypertension, and other conditions that are not pertinent for

most youngsters,” noted Dr. Findling. “Certainly, concerns about tics have been raised in the past,” but a consensus has emerged that stimulants do not commonly cause tics in children without preexisting tics.^{45,46} “As a general rule of thumb,” he continued, “most children do not present any real medical contraindications for the use of psychostimulants. Children are, generally and thankfully, healthy people, which makes them rewarding to treat.”

Long-Acting Stimulants and Drug Holidays.

When selecting medication for the patient with ADHD, the physician must devise a regimen with a rapid and predictable onset of action, an appropriate duration of action, no negative side effects, and a beneficial profile with respect to comorbidities.² Asking the panel to address the use of short- and long-acting stimulant medications, Dr. Salgo inquired, “Are there any potential advantages to be gained by using the long-acting versus short-acting agents?”

“Certainly, a major leap forward has been the ability of longer-acting psychostimulants to preclude the necessity for multiple daily doses of medicine,” declared Dr. Findling, who reviewed the problems inherent in the use of shorter-acting agents. “It can be a real struggle to get a child to take medicine during the school day, which entails being called down to the school nurse and thus being identified as a kid on medicine. In addition, schools are not always cooperative or capable of accommodating these youngsters. Thus, the problems with shorter-acting agents are both emotional, for the children, and administrative, for the schools. Similarly, some of these medicines wear off at the end of the day when kids are getting onto the school bus, a highly unstructured time that can be quite challenging for these children.”

“What about the persistent question of intermittent therapy and drug holidays?” queried Dr. Salgo. “With a longer-acting agent, the options for an intermittent dosing

trial or drug holiday seem to be limited. Is there a role for intermittency or drug holidays with the longer-acting agents?”

“The majority of literature now suggests that drug holidays can be more deleterious than helpful,” replied Dr. Wilens, citing a set of six presentations made at the World Congress of Psychiatry in Berlin in 2005. Five of these presentations demonstrated a very deleterious effect of drug holidays, he reported, while the sixth was equivocal.

“The idea of drug holidays came out of the older literature amid concerns that there were growth delays associated with these medications,” explained Dr. Wilens. “The contemporary literature—in the aggregate, although there is still some controversy—indicates we need not have the dire concerns about effects on height and weight that we once had with these medicines.”

A common tactic, according to the panel, has been to allow children a drug holiday during the summer months, when school is not in session. Dr. Wilens argued against the appropriateness of this approach. “This is a disorder that is constant and chronic, that continues through the summer. Attention is fundamental to navigating life, and these kids are dealing with ADHD all year round. They probably do need treatment throughout the summer months,” he suggested.

Dr. Wilens then turned his attention to differences in prescribing practices among various providers. “It is interesting that child psychiatrists and pediatric neurologists tend not to trail off on their prescriptions for stimulants through the summer. They are relatively consistent through the year. With pediatricians, however, there is a big drop-off—almost a one-third reduction—in the treatment of ADHD through the summer” [IMS proprietary data]. He posited that the message about the deleterious effects of drug holidays “is not being transmitted appropriately or adequately to pediatricians and primary-care physicians from specialists.”

“As a pediatrician myself, I would venture to say that many of my colleagues take

children off their medicines just because it is the way they were trained,” offered Dr. Findling. “Are there some youngsters who do okay with a medicine holiday over the summer? Of course. But if a clinician is going to practice in that fashion, there should be a better rationale than, ‘That is how I was trained.’ ”

Offering an example, Dr. Findling asked readers to consider a child who is going to spend the summer at camp. “If you leave this child unmedicated, will she be able to listen to her counselors and follow instructions so that she enjoys camp? Or is she going to simply suffer unnecessarily? The question to ask is, What is in the best interest of the youngster? There is growing evidence that most children do not benefit from drug holidays.”

Agreeing with his colleague, Dr. Wilens asserted, “As I do more research in this area and have seen patients for almost two decades, I am struck by how frequently problems occur with the withdrawal of the medicines.” To illustrate his point, Dr. Wilens offered a story recently told to him by a pediatrician.

“An eight-year-old girl with inattentive ADHD was taken off her meds for the summer,” he remarked. “She was a reasonable candidate for a drug holiday because most of her problems were with inattention at school and she was doing well socially. The practitioner indicated that, for no apparent reason, this girl walked into the street without thinking and was struck by a car.”

Reminding participants that ADHD is associated with twice the risk of injury and motor vehicle accidents, Dr. Wilens stated, “Unfortunately, these children are plagued by increased risk throughout their lives. Would this girl’s death have been prevented had she continued her stimulant treatment? Nobody can know that, obviously, but when you withdraw a child’s ability to pay attention, they become vulnerable to bad outcomes. Most of the bad outcomes in my practice occur in patients who are not being treated or have stopped taking their medication—not in patients who are on the medication.”

The Role of Nonstimulants. When therapy with stimulants, the first-line treatment for ADHD, fails due to ineffectiveness or intolerance, other medications that have dopaminergic and/or noradrenergic properties may be useful.⁴⁶ The tricyclic antidepressants have proved effective in at least 14 controlled trials,³⁵ but their use can be limited by side effects.⁴⁷ Atomoxetine, a selective noradrenaline reuptake inhibitor, is the first nonstimulant medication to be specifically approved for the treatment of ADHD in children, adolescents, and adults; it has been shown to be safe, well-tolerated, and effective in six published trials in children and adolescents.⁴⁸ Recently, a boxed warning has been added to its product label as a result of concerns that atomoxetine is associated with a small but statistically significant increased risk of suicidal thoughts in children (0.4% with atomoxetine as compared with 0% for placebo).⁴⁹

Moreover, the tricyclic antidepressants and atomoxetine—as well as the novel antidepressant bupropion—produce improvement in all ADHD symptoms clusters just as do the stimulants.⁴⁶ The usefulness of other drug classes—including alpha-adrenergic agents, selective serotonin reuptake inhibitors, and monoamine oxidase inhibitors—is limited by safety concerns and/or insufficient clinical evidence.⁴⁷ Considering this information, asked Dr. Salgo, “How do the nonstimulant medications fit in today’s treatment plans?”

“They are a nice option for certain patients,” answered Dr. Findling, noting that the stimulant and nonstimulant medications have different properties and thus can be matched to a patient’s needs or concerns. “For example, some patients feel that nonstimulants do not have the stigma that stimulants do and so they are more comfortable with them. What the availability of various medicines does is let patients know that there are treatment options. To me, the potential for flexibility is a very nice option for certain patients.”

Offering additional perspective on the nonstimulant medications, Dr. Wilens noted that nonstimulants such as atomoxetine are excellent choices for complex ADHD children such as those with co-occurring tic or anxiety disorders. Nonstimulants may also offer more coverage in the night and early morning.

New Advances in Stimulant Delivery.

Transdermal patch systems have proved to be both effective and innovative in the delivery of medications for a wide range of healthcare purposes. The first transdermal patch system for ADHD utilizes methylphenidate and is designed for once-a-day use in children aged 6 to 12 years. Currently, a new drug application for this methylphenidate transdermal system (MTS) is under review with the US Food and Drug Administration. “The methylphenidate transdermal system is a different treatment strategy altogether,” remarked Dr. Salgo. “What impact might it have on the treatment of patients with ADHD?”

Pointing out that MTS is still under review, Dr. Findling commented that it has several “potential niches should it become available.” One, he noted, “is the fact that it does not require swallowing, a nice advantage for kids who have difficulty swallowing pills.

“Another potential advantage of this form of delivery system,” he added, qualifying that it has not been studied, “is the potential for a flexible duration of action.” He pointed out that, once ingested, both the short-acting and long-acting agents have a fixed and immutable duration of action. The patch, because it can be removed, may permit more flexibility in the duration of action, he suggested.

“Let us say a child sleeps late on the weekend or the parent forgets to give the child his medicine in the morning,” posited Dr. Findling. “You do not want to give a child a 12-hour medicine at noon. The patch might provide the possibility of administration only when wanted.”

Underscoring Dr. Findling's comments, Dr. Wilens offered that "for the first time, we have an off switch. We have flexibility in the duration of action, extending from two hours through 18 hours. With this treatment, we can cover patients who are very busy on, say, Wednesdays, Thursdays, and Fridays and absolutely need coverage all day. As we all know, older teenagers are driving to and from sporting events, practices, and other extracurricular activities. It becomes essential that they be covered, and now they can be. It may translate into some very good or improved outcomes."

"It also uses a very-well-known molecule," pointed out Dr. Manos. "Methylphenidate is very well researched. It is a known entity."

"And the methylphenidate transdermal system has similar tolerability to oral forms of the same medication," noted Dr. Wilens. Noting that methylphenidate is the most studied of the psychostimulants,⁵⁰ Dr. Wilens agreed with Dr. Manos that methylphenidate "is not a novel compound. This is a compound that people are familiar with, with the caveat that the patch delivers more L-isomer. But if you look at methylphenidate's side effect profile on the patch, it is more or less similar to existing methylphenidate delivered in pill form."

In response to a question from Dr. Salgo regarding clinical data, Dr. Findling responded, "There have been some preliminary studies, including two presented at the 2005 annual meeting of the American Academy of Child and Adolescent Psychiatry."⁵¹ Data from these phase II and phase III trials in children aged 6 to 12 years with ADHD showed that MTS was well tolerated and demonstrated statistically significant improvements in primary and secondary endpoints as compared with placebo. In the seven-week phase III trial conducted in 270 children, the declines from baseline in scores on the ADHD Rating Scale were -24.2 in the children randomized to MTS as compared with

-9.9 in the children randomized to placebo ($P < 0.0001$).

Responding to a question about side effects, Dr. Findling remarked, "One of the things that people always ask about with patches is the rate of dermatitis. That does not seem to be a common issue with MTS. In addition, there was a less-than-5% discontinuation rate associated with dermatitis." The most common reported side effects included nausea, vomiting, nasopharyngitis, weight decrease, anorexia, decreased appetite, and insomnia. "The side effect profile looks similar to all methylphenidate compounds, and what is nice about methylphenidate is that it is incredibly predictable," continued Dr. Findling, adding one strategy for managing the side effects of MTS is to simply removing the patch.

Noting that the phase II trial of MTS was an analog classroom study, Dr. Salgo asked Dr. Manos to explain the significance of this method. "The phase II analog classroom study for MTS demonstrated clear behavioral advantage over placebo," stated Dr. Manos. "One of the best measures of whether something has changed as a result of an independent variable or an intervention is frequency of behavior. An analog classroom permits us to make this determination in two ways. First, classroom behavior is monitored, observed, and recorded and, second, a Permanent Product Measure of Performance—which assesses the number of math problems a child completes and the number of math problems a child completes accurately—is taken several times throughout the day." The number of math problems completed and accurate is evidence of the effectiveness of treatment. With the classroom analog method, explained Dr. Manos, "One can get an assessment of how long the duration of action of a particular medicine and how effective it is in improving the behaviors desired in the classroom, at home, and in social settings."

"It seems to me that a potential impact of MTS will be on individualizing treatment and timing treatment," posited Dr. Salgo.

“I believe so,” affirmed Dr. Findling. “Although its effects are not immediate—they depend on the metabolism of the compound—MTS does provide a certain degree of flexibility that is unique. From the beginning of this *Medical Crossfire* we have been talking about tailoring treatment to the individual needs of the youngster with ADHD, and MTS provides yet another important flexible option for the clinician to better meet the needs of certain youngsters.”

Final Thoughts

“ADHD is not a problem of willfulness but is a serious condition that is associated with morbidity and mortality,” declared Dr. Findling in offering a message to take away from this *Medical Crossfire*. “It is pervasive. It is pernicious. But effective treatments are available and need to be considered so that patients do not suffer unnecessarily.”

“People have been suffering with ADHD for a long time, but it is possible now for us to actually treat this disorder,” observed Dr.

Manos. “With the wide use of available interventions, quality of life for many people can be improved.”

“ADHD is a disorder that is associated with impairment, but it is a disorder that can be identified and treated,” emphasized Dr. Wilens. “I have had the experience of treating many pediatric patients with ADHD, and we are seeing good outcomes with proper treatment and a dedicated team that includes the healthcare provider, the family, educators, and other specialists who might be called on as necessary in specific cases.”

Ending the *Medical Crossfire* on an optimistic note, Dr. Wilens observed, “There is something that the health-care provider can do to help children with ADHD. This is an extraordinarily interesting area to be in right now, because there is a great deal of active research as well as emerging therapeutic options such as MTS and other novel approaches. These new tools are going to allow us more options for individualized treatment and optimizing outcomes.” ■

REFERENCES

1. Szatmari P. *The Epidemiology of Attention-Deficit/Hyperactivity Disorder*. Philadelphia, PA: Saunders; 1992:1; 361-371.
2. Szymanski ML, Zolotor A. Attention-deficit/hyperactivity disorder: management. *Am Fam Physician*. 2001;64(8):1355-1362.
3. National Institute of Mental Health. Attention-deficit/hyperactivity disorder. Available at: www.nimh.nih.gov/publicat/ladhd.cfm. Accessed November 1, 2005.
4. Agency for Health Care Policy and Research. Treatment of attention-deficit/hyperactivity disorder. Evidence report/technology assessment: number 11. Available at: www.ahrp.gov. Accessed: November 1, 2005.
5. Practice parameters for the assessment and treatment of attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 1997;36(suppl 10):85S-121S.
6. Barkley RA. Developmental course, adult outcome, and clinic-referred ADHD adults. In: Barkley RA, ed. *Attention-Deficit/Hyperactivity Disorder: A Handbook for Diagnosis and Treatment*, 2nd ed. New York, NY: Guilford Press; 1998:186-224.
7. Elia J, Ambrosini PJ, Rappaport JL. Treatment of attention-deficit/hyperactivity disorder. *N Engl J Med*. 1999;340:780-788.
8. Barkley RA, Fischer M, Edelbrock CS, et al. The adolescent outcome of hyperactive children diagnosed by research criteria: I. An eight-year prospective follow-up study. *J Am Acad Child Adolesc Psychiatry*. 1990;29:546-557.
9. Mannuzza S, Klein RG, Bonagura N, et al. Hyperactive boys almost grown up. V. Replication of psychiatric status. *Arch Gen Psychiatry*. 1991;48:77-83.
10. Gittelman R, Mannuzza S, Shenaker R, et al. Hyperactive boys almost grown up. I. Psychiatric status. *Arch Gen Psychiatry*. 1985;42:937-947.
11. Barkley RA, Guevremont DC, Anastopoulos AD, et al. Driving related risks and outcomes of attention-deficit/hyperactivity disorder in adolescents and young adults: a 3- to 5-year follow-up survey. *Pediatrics*. 1993;92:212-218.
12. Wilens TE, Biederman J, Mick E, et al. Attention deficit hyperactivity disorder (ADHD) is associated with early onset substance use disorders. *J Nerv Ment Dis*. 1997;185(8):475-82.
13. Faraone SV, Perlis RH, Doyle AE, Smoller JW, Goralnick JJ, Holmgren MA, Sklar P. Molecular genetics of attention-deficit/hyperactivity disorder. *Biological Psychiatry* 2005;57:1313-1323.
14. Faraone and Biedman. Presented at USPMH Congress. November 8, 2003.
15. Biederman J, Newcorn J, Sprich S. Comorbidity of attention-deficit/hyperactivity disorder with conduct, depressive, anxiety, and other disorders. *Am J Psychiatry*. 1991;148:564-577.

16. August GJ, Realmuto GM, MacDonald AW 3rd, et al. Prevalence of ADHD and comorbid disorders among elementary school children screened for disruptive behavior. *J Abnorm Child Psychol*. 1996;24:572-595.
17. *Diagnostic and Statistical Manual of Mental Disorders, 4th ed*, text revision. Washington, DC: American Psychiatric Association.
18. Biederman J, Faraone SV, Mick E, et al. Clinical correlates of ADHD in females: findings from a large group of girls ascertained from pediatric and psychiatric referral sources. *J Am Acad Child Adolesc Psychiatry*. 1997;36:1211.
19. Arnold LE. Sex differences in ADHD: conference summary. *J Abnorm Child Psychol*. 1996;24:555-569.
20. Rucklidge JJ, Tannock R. Psychiatric, psychosocial, and cognitive functioning of female adolescents with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2001;40(5):530-540.
21. Blachman DR, Hinshaw SP. Patterns of friendship among girls with and without attention-deficit/hyperactivity disorder. *J Abnorm Psychol*. 2002;30:625.
22. Rucklidge JJ, Tannock R. Psychiatric, psychosocial, and cognitive functioning of female adolescents with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2001;40:530.
23. Conners, et al. ADHD in Adults and Children. Kansas City, MO: Compact Clinicals; 1999.
24. Hinshaw SP. Preadolescent girls with attention-deficit/hyperactivity disorder: I. Background characteristics, comorbidity, cognitive and social functioning, and parenting practices. *J Consult Clin Psychol*. 2002;70(5):1086-1098.
25. Hinshaw SP, Carte ET, Sami N, et al. Preadolescent girls with attention-deficit/hyperactivity disorder: II. Neuropsychological performance in relation to subtypes and individual classification. *J Consult Clin Psychol*. 2002;70(5):1099-1111.
26. Peris TS, Hinshaw SP. Family dynamics and preadolescent girls with ADHD: the relationship between expressed emotion, ADHD symptomatology, and comorbid disruptive behavior. *J Child Psychol Psychiatry*. 2003;44(8):1177-1190.
27. Faraone SV, Biederman J, Mick E, et al. Family study of girls with attention deficit hyperactivity disorder. *Am J Psychiatry*. 2000;157(7):1077-1083.
28. Quinn P, Wigal S. Perceptions of girls and ADHD: results from a national survey. May 2004. Available at: www.medscape.com/viewarticle/472415_1. Accessed November 2, 2005.
29. Brown RT, Freeman WS, Perrin JM, et al. Prevalence and assessment of attention-deficit/hyperactivity disorder in primary care settings. *Pediatrics*. 2001;107(3):E43.
30. Abikoff H, Hechtman L, Klein RG, et al. *J Am Acad Child Adolesc Psychiatry*. 2004;43:820-829.
31. Hechtman L, Abikoff H, Klein RG, et al. *J Am Acad Child Adolesc Psychiatry*. 2004;43:812-819.
32. Pelham WE, Murphy HA. Behavioral and pharmacological treatment of hyperactivity and attention-deficit disorders. In: Herson M, Breuning SE, eds. *Pharmacological and Behavioral Treatment: An Integrative Approach*. New York, NY: John Wiley & Sons; 1986:108-147.
33. Hinshaw SP, Klein RG, Abikoff H. Childhood attention-deficit/hyperactivity disorder: nonpharmacologic and combination treatments. In: Nathan PE, Gorman JM, eds. *A Guide to Treatments that Work*. New York, NY: Oxford University Press; 1998:26-41.
34. Pelham WE, Wheeler T, Chronis A. Empirically supported psychosocial treatments for attention-deficit/hyperactivity disorder. *J Clin Child Psychol*. 1998;27:190-205.
35. Barkley RA, Edwards G, Laneri M, et al. The efficacy of problem-solving communication training alone, behavior management training alone, and their combination for parent-adolescent conflict in teenagers with ADHD and ODD. *J Consult Clin Psychol*. 2001;69(6):926-941.
36. Chronis, AM et al (2004). Enhancements to the behavioral parent training paradigm for families of children with ADHD: Review and future directions. *Clinical child and family psychology review*, 7, 1-27.
37. Madsen, CH, Becker WC, & Thomas DR. Rules, praise, and ignoring: Elements of elementary classroom control. *J Applied Behavior Analysis*. 1968; 1:139-150.
38. The MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry*. 1999;56:1073-1086.
39. Bradley C. Behavior of children receiving benzedrine. *Am J Psychiatry*. 1937;94:577-585.
40. Goldman LS, Genel M, Bezman RJ, et al. Diagnosis and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *JAMA*. 1998;279:1100-1107.
41. Wilens TE, Faraone SV, Biederman J, Gunawardene S. Does stimulant therapy beget later substance abuse? A meta-analytic review of the literature. *Pediatrics*. 2003;111(1):179-185.
42. Gillberg C, Melander H, von Knorring, et al. Long-term stimulant treatment of children with attention-deficit/hyperactivity disorder symptoms. *Arch Gen Psychiatry*. 1997;54:857-864.
43. Klorman R, Brumaghin JT, Fitzpatrick PA, Borgstedt AD. Clinical effects of a controlled trial of methylphenidate on adolescents with attention deficit disorder. *J Am Acad Child Adolesc Psychiatry*, 1990;29:702-709.
44. Barkley RA, DuPaul GJ, McMurray MB. Attention-deficit disorder with and without hyperactivity: clinical response to three dose levels of methylphenidate. *Pediatrics*. 1991;87:519-531.
45. Law SF, Schachar RJ. Do typical doses of methylphenidate cause tics in children treated for attention-deficit hyperactivity disorder? *J Am Acad Child Adolesc Psychiatry*. 1999;38:944-951.
46. ADHD: what to do when stimulant treatment fails. *Neuropsychiatry Rev*. 2002;3(2):1-7.
47. Banaschewski T, Roessner V, Dittmann RW, et al. Nonstimulant medications in the treatment of ADHD. *Eur Child Adolesc Psychiatry*. 2004;13(suppl 1):102-116.
48. Y. Corman SL, Fedutes BA, Culley CM. Atomoxetine: the first nonstimulant for the management of attention-deficit/hyperactivity disorder. *Am J Health Syst Pharm*. 2004;61(22):2391-2399.
49. Lilly Announces Important Strattera Label Update [press release]. September 29, 2005. Available at: newsroom.lilly.com/ReleaseDetail.cfm?ReleaseID=175142. Accessed November 10, 2005.
50. Wilens TE, Spencer TJ. The stimulants revisited. *Child Adolesc Psychiatry Clin North Am*. 2000;9(3):573-603.
51. Data presented at: 52nd annual meeting of the American Academy of Child and Adolescent Psychiatry; Toronto, Ontario, Canada; Oct 20-21, 2005.

Identification and Discussion of Key Issues and Advances in Pediatric ADHD

CME Test

- Which of the following are *not* affected by ADHD if left untreated?
 - level of achievement
 - self-esteem
 - interpersonal relationships
 - All of the above are affected by ADHD.
- The presence of comorbidity in children with ADHD is
 - rare.
 - infrequent.
 - common.
 - not well studied.
- The course of ADHD is affected by two factors: one is pleomorphism, or natural change in symptoms; the other is
 - the efficacy of treatment.
 - the stability of the home environment.
 - the effect of hormonal changes.
 - the introduction of new demands.
- Girls with ADHD are more likely than boys with the disorder to demonstrate
 - oppositional disorder.
 - depression.
 - a learning disability.
 - sense of a loss of control.
- Which of the following will not be helpful in diagnosing ADHD?
 - clinical interviews
 - assessment instruments
 - laboratory tests
 - All of the above were pointed out by the panel as useful in making a diagnosis of ADHD.
- Which of the following psychotherapeutic interventions has not been demonstrated to be effective in the treatment of ADHD specifically?
 - cognitive-behavioral therapy
 - behavioral therapy
 - social skills training
 - parent skills training
- In the management of pediatric ADHD, the primary purpose of behavior modification is
 - to correct the negative behaviors of children.
 - to encourage the positive behaviors of children.
 - to change the behaviors of parents and teachers.
 - to improve the communication between adults and children.
- According to the expert panel, what is the primary benefit of the longer-acting stimulants?
 - greater efficacy
 - fewer side effects
 - better cost-effectiveness
 - negates the need for multiple daily doses of medicine
- Which of the following best reflects the current thinking in regard to drug holidays for children with ADHD?
 - Drug holidays are beneficial to ensure normal physical growth.
 - Drug holidays should be considered in children with inattentive-type ADHD.
 - Drug holidays should be considered only in specific children who are doing well socially and academically.
 - Drug holidays are more deleterious than helpful.
- According to the faculty, what might be the primary benefit of a transdermal patch system for treating children with ADHD?
 - greater efficacy
 - fewer side effects
 - better acceptance by children
 - flexible duration of action

Identification and Discussion of Key Issues and Advances in Pediatric ADHD

CME Registration and Evaluation Form

In order to obtain AMA/PRA category 1 credit, participants are required to

1. Read the learning objectives, review the activity, and complete the self-assessment test.
2. Complete the registration and evaluation form and record your answers in the box to the right.
3. Send the activity registration and evaluation form to:
UMDNJ–Center for Continuing and Outreach Education
via mail: P.O. Box 1709, Newark, NJ 07101-1709 or
via fax: (973) 972-7128

A continuing education credit letter will be mailed to you within 3 to 4 weeks. Credit for this activity is available until March 31, 2007.

Program Objectives

Having completed this activity, are you better able to:

| | Strongly Agree | | | Strongly Disagree |
|---|----------------|---|---|-------------------|
| Review important aspects of the clinical picture of pediatric ADHD in patients at various stages of development. | 5 | 4 | 3 | 2 1 |
| Describe the role of multimodal strategies of treating pediatric patients with ADHD. | 5 | 4 | 3 | 2 1 |
| Discuss strategies for optimizing the use of currently available therapies in the management of pediatric ADHD. | 5 | 4 | 3 | 2 1 |
| Consider the potential impact that advances in therapeutic strategies may have on clinicians' ability to individualize treatment. | 5 | 4 | 3 | 2 1 |

Overall Evaluation

| | Strongly Agree | | | Strongly Disagree |
|--|----------------|---|---|-------------------|
| The information presented increased my awareness/understanding of the subject. | 5 | 4 | 3 | 2 1 |
| The information presented will influence how I practice. | 5 | 4 | 3 | 2 1 |
| The information presented will help me improve patient care. | 5 | 4 | 3 | 2 1 |
| The faculty demonstrated current knowledge of the subject. | 5 | 4 | 3 | 2 1 |
| The activity was educationally sound and scientifically balanced. | 5 | 4 | 3 | 2 1 |
| The activity avoided commercial bias or influence. | 5 | 4 | 3 | 2 1 |
| Overall, the activity met my expectations. | 5 | 4 | 3 | 2 1 |
| I would recommend this activity to my colleagues. | 5 | 4 | 3 | 2 1 |

If you anticipate changing one or more aspects of your practice as a result of your participation in this activity, please provide us with a brief description of how you plan to do so. You may attach a separate piece of paper.

Please provide any additional comments pertaining to this activity (positives and negatives) and suggestions for improvement.

Please list any topics that you would like to be addressed in future educational activities.

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Self-Assessment Test

Circle the best answer for each question on the CME test.

- | | | | | |
|-----|---|---|---|---|
| 1. | A | B | C | D |
| 2. | A | B | C | D |
| 3. | A | B | C | D |
| 4. | A | B | C | D |
| 5. | A | B | C | D |
| 6. | A | B | C | D |
| 7. | A | B | C | D |
| 8. | A | B | C | D |
| 9. | A | B | C | D |
| 10. | A | B | C | D |

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1. d. According to Dr. Wilens, self-esteem, a patient's ability to achieve, and interpersonal relationships are all affected by ADHD.

Locator: Current Perspectives/The Burden of ADHD

2. c. Approximately 65% of children with ADHD have at least one other comorbid condition, including depression, conduct disorder, oppositional defiant disorder, Tourette's syndrome, and learning disabilities, among others.

Locator: Recognizing and Diagnosing ADHD

3. d. Pleomorphism is demonstrated in ADHD by the natural diminution of symptoms of hyperactivity and impulsivity as children age. This natural change in symptoms is compounded when new demands are made on children as they develop. For example, the introduction of more-challenging cognitive tasks in the higher academic grades may impact the course of ADHD.

Locator: Recognizing and Diagnosing ADHD/When is it ADHD?

4. d. "Girls, in general, lose a sense of inner locus of control—that is, the sense that they control their lives and control the circumstances of their lives," explained Dr. Manos. This loss occurs more frequently and at an earlier age in girls with ADHD as compared with both boys with ADHD and normal girls, he added. Dr. Wilens cautioned that, despite a few differences, "There are a lot more similarities than dissimilarities between the genders when it comes to ADHD. We need to focus attention on girls and realize that girls as well as boys have the disorder."

Locator: Recognizing and Diagnosing ADHD/Gender Issues in ADHD

5. c. The diagnosis of ADHD is a clinical one and must rely on a combination of clinical interviews and assessment instruments. There are no laboratory tests available for making this diagnosis.

Locator: Recognizing and Diagnosing ADHD/Insights into Diagnosis

6. a. Cognitive-behavioral therapy (CBT) is very effective for comorbid disorders such as depression, anxiety, and adjustment disorders, observed Dr. Manos; however, "using CBT to treat symptoms of ADHD has not been effective." Fortunately, several other psychotherapeutic interventions can be helpful in ameliorating symptoms of pediatric ADHD.

Locator: Strategies for the Successful Management of ADHD/Current Issues in Psychotherapy

7. c. Dr. Manos emphasized, "Behavior modification is not about changing behavior in children. That happens secondarily. It is about changing behavior in the change agents around the child, which largely means parents and teachers."

Locator: Strategies for the Successful Management of ADHD/Current Issues in Psychotherapy

8. d. "Certainly, a major leap forward has been the ability of longer-acting psychostimulants to preclude the necessity for multiple daily doses of medicine," declared Dr. Findling, who added that the problems with multiple daily dosing of short-acting agents are of an emotional nature for the child and an administrative nature for the child's school.

Locator: Strategies for the Successful Management of ADHD/Current Issues in Pharmacotherapy/Long-Acting Stimulants and Drug Holidays

9. d. "The weight of the literature now is that drug holidays can be more deleterious than helpful," advised Dr. Wilens. "This is a disorder that is constant and chronic, that continues through the summer," he explained. "Attention is fundamental to navigating life, and these kids are dealing with ADHD all year round."

Locator: Strategies for the Successful Management of ADHD/Current Issues in Pharmacotherapy/Long-Acting Stimulants and Drug Holidays

10. d. A transdermal patch system, because it can be removed and replaced, may permit more flexibility in the duration of action, suggested Dr. Findling. Agreeing with his colleague, Dr. Wilens stated, "This is the first time, to my knowledge, that we have an on-off switch whereby we can turn the medication on and off as necessary."

Locator: Strategies for the Successful Management of ADHD/Current Issues in Pharmacotherapy/New Advances in Stimulant Delivery