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## What Is Attention-Deficit Hyperactivity Disorder (ADHD)?

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### Abstract

Attention-deficit hyperactivity disorder (ADHD) is described as the most common neurobehavioral condition of childhood. We raise the concern that ADHD is not a disease per se but rather a group of symptoms representing a final common behavioral pathway for a gamut of emotional, psychological, and/or learning problems. Increasing numbers of children, especially boys, are diagnosed with ADHD and treated with stimulant medications according to a simplified approach. Methodical review of the literature, however, raised concerning issues. "Core" ADHD symptoms of inattentiveness, hyperactivity and impulsivity are not unique to ADHD. Rates of "comorbid" psychiatric and learning problems, including depression and anxiety, range from 12 to 60%, with significant symptom overlap with ADHD, difficulties in diagnosis, and evidence-based treatment methods that do not include stimulant medications. No neuropsychologic test result is pathognomic for ADHD, and structural and functional neuroimaging studies have not identified a unique etiology for ADHD. No genetic marker has been consistently identified, and heritability studies are confounded by familial environmental factors. The validity of the Conners' Rating Scale-Revised has been seriously questioned, and parent and teacher "ratings" of school children are frequently discrepant, suggesting that use of subjective informant data via scale or interview does not form an objective basis for diagnosis of ADHD. Empiric diagnostic trials of stimulant medication that produce a behavioral response have been shown not to distinguish between children with and without "ADHD." In summary, the working dogma that ADHD is a disease or neurobehavioral condition does not at this time hold up to scrutiny of evidence. Thorough evaluation of symptomatic children should be individualized, and include assessment of educational, psychologic, psychiatric, and family needs.

### Article Content

Attention-deficit hyperactivity disorder (ADHD) has become a common diagnosis in the United States, with reported rates in school-aged boys and girls of approximately 10% and 4%, respectively, and increasing numbers of children on stimulant medications. Professional organizations, including the American Academy of Pediatrics and the American Academy of Child and Adolescent Psychiatry, have issued consensus statements on the evaluation and treatment of ADHD, and most physicians accept ADHD as a diagnostic entity.<sup>[1-4]</sup> Many teachers and parents also readily apply this label to children in their care. ADHD is described as the "most common neurobehavioral disorder of childhood."<sup>[1]</sup> Before we permit ourselves to ride this "tidal wave" of apparent agreement, it might be helpful to critically review underlying evidence and suppositions. What, really, is ADHD? Is ADHD a collection of symptoms, or is it a disease entity? Who is qualified to diagnose, evaluate, and treat these symptoms or this condition?

At first blush, the American Academy of Pediatrics guidelines would seem to provide a blanket of comfort to the beleaguered primary care physician. They define the "core symptoms" of ADHD as "inattentiveness, impulsivity and hyperactivity" and urge clinicians to use the *Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)* criteria to make a diagnosis.<sup>[5]</sup> The guidelines acknowledge that there is no objective test or identified etiology for ADHD and that diagnosis relies on subjective criteria. Pediatricians are directed to assess for "comorbidities," such as major affective disorders and learning problems. They should then begin treatment of diagnosed children with "stimulant medications and/or behavioral treatment" after "negotiating target outcomes."<sup>[2]</sup> The guidelines are concrete and appear to codify what many pediatricians think they are already doing. However, a recent study found that only 25.8% of pediatricians "reported routine use of all 4 diagnostic components" and only 53.1% performed follow-up visits three to four times per year, as recommended for their patients on stimulant medications.<sup>[6]</sup> There must be obstacles to use of the guidelines, and it is reasonable to examine assumptions underlying both the guidelines and the "diagnosis" of ADHD.

Concern has been raised that symptoms or groups of symptoms do not constitute a diagnosis and that the core symptoms of ADHD do not constitute a diagnostic entity.<sup>[7-10]</sup> Pediatricians are trained to evaluate signs and symptoms to reach a differential diagnosis. Cough and fever are obvious examples of prominent symptoms that are not diagnoses in themselves. Although codeine suppresses cough and ibuprofen suppresses fever, treatment of symptoms is not the primary or only diagnostic and therapeutic approach. Either cough or fever can be due to a concerning underlying condition or to a fleeting minor ailment, and evaluation will be based on the details of the child's history and physical examination. To make a diagnosis, testing (such as a chest radiograph or blood counts) and follow-up might be needed. Few clinicians would consider using suppressive medications (such as codeine and ibuprofen) for longer than a brief finite period, and most would worry about missing a treatable and/or less common underlying diagnosis, such as malignancy or pneumonia. Thus, there is no model within primary care for basing diagnosis and treatment on symptoms alone, and the recommended approach to ADHD runs counter to most pediatricians' formal training.

Following the "symptoms do not constitute a diagnosis" logic leads us in two immediate directions. First, several authors have considered other hypotheses regarding the core symptoms of inattention, distractibility, and hyperactivity, including the possibilities that this behavior represents (1) one end of a normal distribution of school-aged behavior (especially for boys, who are overrepresented in every study), (2) an expression of endogenous temperament, (3) differences in rates of developmental maturation, or (4) rigid or unreasonable parental, societal, or educational expectations for school-aged children.<sup>[10-18]</sup> Since a relatively high percentage of children are identified in cross-sectional studies as having core symptoms, it would be interesting to study whether an equally high percentage of children could be identified as having "overattention and hypoactivity" beyond 2 SD for age on the other end of a normal distribution of behavior for school-aged children.<sup>[19,20]</sup> Obviously, this study has not been done and is unlikely to be done because these children do not cause disruption or behavior management problems.

Second, we need to examine the possibility that for some or many children, the core symptoms of ADHD are neither a normal variant nor a defined disease state. These symptoms might represent expressions of internalized conflict or unmet emotional or educational needs that differ from child to child. In this scenario, each child should have a full medical, educational, and psychologic or psychiatric evaluation. The American Academy of Child and Adolescent Psychiatry previously formally recommended as an initial evaluation (1) an interview with the parents (to include the child's and the family's history); (2) use of standardized rating scales; (3) school information, including the results of academic testing; (4) a (psychiatric) child diagnostic interview; (5) a family diagnostic interview; (6) a complete physical examination; and (7) referral for additional testing as needed.<sup>[21]</sup> In this approach, multiple diagnoses are actively considered, including psychiatric and affective disorders, educational and learning disorders, and family psychopathology, ranging from stress following a divorce or bereavement to domestic violence, abuse, and substance abuse. This comprehensive approach has been condensed beyond recognition in the American Academy of Pediatrics guidelines, which direct the pediatrician to obtain qualitative information from school and parents, make a diagnosis of ADHD based on *DSM-IV* criteria, and "evaluate for co-existing conditions...although the pediatrician might not always be in a position to make a precise diagnosis [of the same]."<sup>[1]</sup> The guidelines do not recommend referral to mental health or educational specialists. The new American Academy of Pediatrics approach thus offers an expedited but significantly less comprehensive approach to symptom evaluation.

One significant obstacle to acceptance of ADHD as a "neurobehavioral" disease entity is the lack of evidence of an underlying unique genetic, neurologic, psychologic, or biologic pathology and the lack of an identified etiology. Work showing the "heritability" of ADHD suffers from difficulty distinguishing genetic heritability, which has not been proven, from environmental and parenting influences. No genetic marker has been consistently identified, despite extensive study of putative genes in the dopaminergic, serotonergic, and noradrenergic system.<sup>[22-26]</sup> Interpretation of twin studies is confounded by environmental influences.<sup>[27,28]</sup> A recent review article concluded that "more work from twin and molecular genetic studies is needed to determine if the increased familiarity of persistent ADHD reflects the actions of genes or of familial environmental causes."<sup>[29]</sup> "Environmental influences" are associated with ADHD and include lower socioeconomic status, maternal psychopathology, and family conflict.<sup>[26]</sup> In younger children (ages 3-7 years), maternal anxiety and mood disorders, substance abuse, and other psychopathology, including parental childhood ADHD symptoms and disruptive behavior, are each associated with the diagnosis of ADHD; others have reported similar findings in older children diagnosed with ADHD.<sup>[30-32]</sup> A recent study examining correlates of comorbid psychopathology in 300 referred children with a "confirmed" diagnosis of ADHD (mean age 10.7 years; 83.3% boys) found a 19.3% rate of parental antisocial or criminal behavior, defined as an arrest for other than a motor vehicle violation, and a 30% rate of parental substance abuse.<sup>[33]</sup>

Deficits in "executive function" have been postulated as a cause of ADHD or at least as a prominent disturbance. Executive functioning is defined differently by different authors but broadly includes the ability to self-monitor, stay focused in the face of interference, think flexibly, and organize oneself. Although corresponding deficits on neuropsychologic testing "that likely require the interaction of several executive functions for adequate performance" have been identified (in addition to specific cognitive deficits in other

domains), there is no single profile that is diagnostic or pathognomonic for ADHD, and "many of the cognitive deficits seen in ADHD also are observed in other neurodevelopmental disorders."<sup>[27]</sup>

"Executive function" is currently thought to be located in five pathways in the frontostriatocortical circuitry that connects the subcortical areas to the frontal lobe. Structural neuroimaging with computed tomography (CT) and magnetic resonance imaging (MRI) has shown volumetric changes in these areas, including the cerebellum, frontal lobe, and other cortical and subcortical regions, but the changes are inconsistent from study to study and are not uniformly right or left sided.<sup>[34-39]</sup> Studies showing structural differences on neuroimaging scans between "ADHD children" and controls suffer from small sample sizes, heterogeneous and noncomparable control groups, a lack of replication, use of cross-sectional rather than longitudinal data, and a lack of distinction between results that show an association and those that demonstrate cause and effect. A recent review of research using electroencephalography and MRI in the study of ADHD concluded that, regarding "theories of ADHD that focus on a fronto-striatal neurological circuitry substrate..., the specificity of this finding for ADHD, remain[s] unresolved."<sup>[40]</sup>

"Structure-function" correlations have been attempted in which children with and without ADHD are tested on two to three attentional tasks and then scanned with cranial MRI.<sup>[41,42]</sup> These studies also suffer from small sample sizes, use of highly selected subjects, conflicting results, and a lack of replication. The author of one study concluded that "the associations between attentional performance and MRI-based anatomical measures of structure size are crude."<sup>[42]</sup> Functional neuroimaging studies using positron emission tomography and single-photon emission computed tomography (SPECT) have also been conducted.<sup>[43,44]</sup> In addition to the problems noted above, these studies have variably included control groups with symptoms overlapping the ADHD group, have compared groups on an outcomes measure (<sup>99m</sup>Tc-HMPAO brain SPECT) known to be normal in one group, and, most significantly, speculate but cannot document a causal relationship between hypoperfusion of given regions of the brain and "hypofunction" of those regions. To quote Roth and Saykin, "the specificity of [the] structural and functional neuroimaging findings to ADHD is [also] largely unknown."<sup>[27]</sup>

Meanwhile, longitudinal studies have shown that myelination of individual areas of the brain occurs at different ages and different rates and that intracortical association might not mature until the midtwenties.<sup>[45]</sup> The frontal lobes are among the last regions to become functionally and anatomically mature, and maturation peaks at ages 10.5 years and again between ages 17 and 21 years.<sup>[46-48]</sup> The work of Bunge and colleagues, who performed functional MRI on both child and adult subjects, suggests that the direct "lesion = symptom" hypothesis might be grossly oversimplified. Although their studies were not longitudinal, they found that children and adults not only performed differently (eg, children were more susceptible to interference on tasks) but also exhibited different patterns of cortical activation.<sup>[49]</sup> Children showed "immature prefrontal activation that varied according to the type of cognitive control required."<sup>[49]</sup> In other words, there appear to be developmental changes in both clinical responses and in patterns of cortical activation associated with age and task. Whether different patterns of activation are also related to chronic or situational stress, gender, or other influences is not known. Thus, although patterns of cortical activation might be associated with patterns of behavior on testing, such relationships are complex, confounded by age and possibly other factors, and do not identify a biologic etiology for the symptoms of ADHD.

In summary, neither structural or functional neuroimaging, neuropsychologic testing, nor genetic testing offers more than correlations between ADHD symptoms and test results, and most studies have not been replicated. An underlying cause has not been defined, although several have been hypothesized.

In the absence of an identified underlying biologic mechanism or etiology for ADHD that would support a diagnostic test, clinicians are asked to use criteria and rating scales. What rating scales are available to clinicians? Psychiatrists and psychologists use a variety of techniques to identify pathology, including full and structured interview and other diagnostic tools, whereas pediatricians have less familiarity with psychiatric diagnostic assessment. The American Academy of Child and Adolescent Psychiatry lists seven "Common Rating Scales" for assessing symptoms of ADHD in children in addition to the Conners' Parent and Teacher Rating Scales-Revised.<sup>[4,50]</sup> The American Academy of Pediatrics list of "ADHD-specific Checklists" includes only the familiar Conners' parent and teacher rating scales for children ages 6 to 17 years and an additional scale for girls only (the SSQ-O-I Barkley's School Situations questionnaire).<sup>[1]</sup> The American Academy of Pediatrics guidelines caution the clinician that these scales, which are described as able to "distinguish between children with and without the diagnosis of ADHD," were tested under "ideal" conditions and "may function less well in primary care clinicians' offices" and that "[the] questions on which these rating scales are based are subjective and subject to bias."<sup>[1]</sup> This realistic assessment of the rating scales is borne out by further evaluation.

Research on the original Conners' rating scales showed high correlations (0.49-0.68) between items on the teacher's scale, indicating that factors are not independent, and a high correlation on the parents' scale between conduct problems and hyperactivity (0.55), suggesting the same problem.<sup>[13,51]</sup> Although the newer Conners' Rating Scales-Revised are recommended, some clinicians continue to use the older version. A recent review by

Collett and colleagues concluded that rating scales can "reliably, validly and efficiently measure *DSM-IV* based ADHD symptoms in youth," but a careful review of the statistical methods used to reach this conclusion makes it extremely doubtful.<sup>[52,53]</sup> Only two of the nine measures examined were tested for validity, which is the crucial question, that is, does the rating scale actually measure what we are trying to measure? Specifically, the same population was used to both develop and validate the Conners' Rating Scale, which represents a profound statistical oversight. Normative data for the Conners' Rating Scale-Revised are limited.<sup>[54]</sup> The only other ADHD rating scale evaluated for validity (the ADHD-IV) "faired poorly with the specificity ranging as low as random chance (49%)."<sup>[53]</sup> In a letter critiquing the analysis, Snyder et al stated:

In the use of rating scales, the act of applying a cutoff and assigning qualitative (clinical) meaning to a score requires specific statistical tests to confirm the validity of the scale as used in common practice. Considering the insubstantial results of the two rating scales [Conners and ADHD-IV] that were tested for criterion validity and the lack of such testing of the other nine reviewed scales, Collett et al lack sufficient evidence to conclude that rating scales can validly measure *DSM-IV*-based ADHD symptoms.<sup>[53]</sup>

Although this conclusion can be debated, it cannot be ignored. The Conners' Rating Scale-Revised, which pediatricians commonly use and are directed to use for diagnosis and monitoring, has not yet been proven to measure ADHD symptoms.

The use of the *DSM-IV* criteria for the diagnosis of ADHD is promoted. Why not accept ADHD as a psychiatric diagnosis that primary care physicians can make based on listed criteria? The major difficulty is that the diagnostic criteria are neither "normed" nor quantified. Judgment and experience are needed to appreciate what is "usual" for a 7-year-old or a 10-year-old or a 14-year-old boy or girl. The impact of subjectivity on symptom assessment is considerable. Revised *DSM-IV* criteria for ADHD require that children suffer impairment from their symptoms in more than one setting, and the American Academy of Pediatrics guidelines recommend obtaining information from both the parent and the teacher.<sup>[1,5]</sup> It is well known, however, that there are frequent and significant discrepancies between parent and teacher ratings of children being evaluated for ADHD.<sup>[55]</sup> Safer noted: "The agreement between parent and teacher informants on the features of ADHD is quite low in virtually all studies."<sup>[56]</sup> For example, Mitsis et al examined 74 clinically referred children and found that "parent and teacher agreement regarding the presence of individual symptoms in the school setting was rarely better than chance" and that "agreement between parents and teachers on structured diagnostic interview regarding the categorical diagnoses of ADHD...is relatively poor."<sup>[57]</sup> The American Academy of Pediatrics guidelines suggest that these discrepancies might be due to differences between settings in "expectations, levels of structure, behavioral management strategies, and/or environmental circumstances."<sup>[1]</sup> If these factors do impact behavior and symptom expression (eg, attentiveness, level of activity), which most providers would acknowledge, it becomes more difficult to attribute symptoms to an intrinsic disease condition. School referrals are more frequent than parent referrals and are more likely to agree with physician diagnosis of ADHD.<sup>[58-61]</sup> In a study from the United Kingdom regarding use of mental health services for hyperactivity, the strongest predictor of a parent's perception that the child's hyperactivity was a problem meriting referral was the financial impact of the child's behavior on either parent's work.<sup>[62]</sup> These and other data and many clinicians' anecdotal experiences suggest that the disruptiveness of a child's behavior to school or home routine is the driving force for referrals; thus, subjective assessment of the child's behavior is unlikely to be an objective diagnostic tool.

The issue of comorbid conditions is addressed in the American Academy of Pediatrics guidelines, although a comprehensive plan with which to identify the conditions is not included. Study after study documents a significant rate of comorbid psychiatric conditions in children diagnosed with ADHD.<sup>[63-65]</sup> These coexisting conditions include problems with parent-child interaction, family violence, and parental psychopathology, as well as childhood anxiety; mood disorders, including mania, bipolar disorder, and depression; learning disabilities; conduct disorder; and oppositional defiant disorder. Estimates of the rates of these comorbid conditions range from 35% to 60% for oppositional or conduct disorder, from 12% to 60% for learning disabilities, from 18% to 60% for mood disorders, including major depression, and from 25% to 34% for anxiety disorders.<sup>[66-75]</sup> In nonreferral populations, it can be difficult to accurately ascertain the rates of comorbid conditions because most primary care practitioners are not trained to make these assessments. The diagnosis of comorbid conditions is critical because such psychopathology "may influence severity, daily functioning, treatment, and prognosis" and "is associated with significant additional morbidity and [that] complicates the diagnosis, treatment, and prognosis of ADHD."<sup>[76,77]</sup>

The difficulties in diagnosing and treating comorbid conditions are not trivial. For example, Plizka stated that "almost all children younger than 12 years of age who meet criteria for [oppositional defiant disorder] or [conduct disorder] will almost always meet criteria for ADHD."<sup>[67]</sup> Stimulants are reported to be efficacious for all three conditions, although children with conduct disorder can have "aggressive outbursts" and require additional intervention, particularly when there is significant family psychopathology.<sup>[78,79]</sup>

Regarding educational comorbidities, learning disability and ADHD are reported to be completely separate conditions, although learning disability (and/or low cognitive ability) can lead to inattention and frustration in the classroom and thus masquerade as ADHD. Children with reading disability and ADHD who are treated with stimulants show improvement in reading scores, whereas those with reading disability alone do not; this finding is used to support a strategy of treating all inattentive students who have academic failure with stimulant medication.<sup>[80-82]</sup> An alternative diagnostic strategy would be to perform psychometric testing for children with academic problems; several authors suggest that this would be the ideal approach because educational interventions are the treatment of choice for learning problems. There is good evidence that stimulant medications do not improve learning per se but rather improve performance on tasks requiring repetition and concentration.<sup>[83-85]</sup>

One of the most difficult and controversial areas in pediatric mental health is making the diagnosis in children of depression and other major affective disorders, including bipolar disorder.<sup>[86-88]</sup> A recent consensus statement concluded that there are high rates of unmet needs for children and adolescents with depression or bipolar disorder and that training in diagnosis and treatment is largely limited to child mental health specialists, with general practitioners, including pediatricians, receiving little or no training.<sup>[86]</sup> According to national data, "more than 70% of children and adolescents with serious mood disorders are either undiagnosed or inadequately treated," and owing to the strong continuity of childhood mood disorders with adult mood disorders, this deficit has broad implications.<sup>[86,87,89,90]</sup> Since the *DSM-IV* criteria were derived from adult studies, their applicability to children is questioned, and diagnosis at least requires the input of both the parent and the child if the child is under the age of 14 years. The consensus statement concluded that validated and developmentally appropriate methods of diagnosis are needed, as well as trials of antidepressants, mood stabilizers, and psychotherapeutic interventions in pediatric and adolescent populations. Stimulants are not a recommended treatment for major affective disorders and can cause dysphoria or harmful mood dysregulation. Specifically with regard to bipolar disorder, a recent consensus panel recommended "to carefully use the stimulants [in a child with 'coexisting ADHD'] if clinically indicated and *only after* [my italics] the child's bipolar symptomatology has been controlled with a mood stabilizer."<sup>[91]</sup> The combination of difficulties in both diagnosing and treating depression makes this comorbidity a potential minefield for the primary provider not specifically trained in mental health care.

The comorbid symptoms of anxiety have received less attention but occur frequently. In the Multimodal Treatment Study of ADHD (MTA) study, 34% of children with diagnosed ADHD also met full criteria for an anxiety disorder, and Wilens et al found multiple (more than two) anxiety disorders in 127 (33%) of 381 school-aged children with ADHD referred to their consultation clinic.<sup>[68,69]</sup> Possibly since anxiety is an "internalizing disorder," compared with the more visible ("externalizing") symptoms of conduct disorder and inattention, information from teachers is less likely to contribute to its identification.<sup>[92]</sup> Also, children and their parents frequently do not concur in their assessments: the child feels anxious, and the adult does not perceive this, or vice versa.<sup>[67,93]</sup> This does not mean that anxiety symptoms are unimportant; not only does the child with anxiety symptoms suffer psychologically, but there is also strong evidence that symptoms of anxiety disorders predict major depression and bipolar disorder.<sup>[86,94-96]</sup> Studies have evaluated the differential response to stimulant medications of children with ADHD with and without symptoms of anxiety. Most studies, although not all, show that significantly fewer children with anxiety compared with those without anxiety respond to stimulants (30% compared with 80% in a double-blinded study).<sup>[97-100]</sup> In the MTA study, psychosocial treatment in addition to medication benefited the anxious children with ADHD more than the nonanxious children with ADHD.<sup>[68]</sup> A recent review concluded that "from an evidence-based perspective, cognitive-behavioral therapy is currently the treatment of choice for anxiety [and depressive disorder] in children and adolescents."<sup>[101]</sup> Thus, the treatment of choice for anxiety is not stimulants, and children with anxiety and the ADHD diagnosis do not respond as well to stimulants. Unfortunately, most primary providers are not trained to assess children for anxiety and will be unlikely to provide these children with optimal treatment.

In summary, the prominent and often complete symptom overlap of ADHD with other psychopathology and the difficulties distinguishing ADHD from other pathology can be viewed as supporting the thesis that ADHD is not a distinct neurologic or psychologic disease entity. Instead, the symptoms of hyperactivity, inattention, and impulsivity might represent a final common behavioral pathway for a gamut of emotional, psychologic, and/or learning problems. Clinical experience and case studies reveal that other problems, for example, occult mental retardation, hypervigilance owing to fear or stress, and ongoing or past abuse, can masquerade as ADHD.<sup>[8,102,103]</sup> The primary care provider without a specific mental health background is not trained to identify or diagnose most conditions considered "comorbid" with ADHD, and most do not have the time or experience to fully evaluate educational and psychiatric concerns. Stimulant medication is neither the primary nor the recommended treatment for each of these conditions, can actually be harmful in some (eg, major mood disorders), and does not treat the underlying problem in others (eg, anxiety, abuse).

The use of stimulant medications in children with symptoms of hyperactivity and inattention is promoted by some as a diagnostic trial. The working plan is that if the child looks, acts, or functions better on a stimulant medication, then he or she should be on the medication, and a diagnosis of ADHD has been confirmed. The choice of actual medication and dose is highly empiric because there is no current method of determining

whether an amphetamine or a methylphenidate (or the nonstimulant amoxetine) will be "better" for an individual patient. However, studies have shown that behavioral response to stimulants does not distinguish children with diagnosed ADHD from normal children; thus, a behavioral response does not constitute either a diagnosis or a treatment but rather an expected response to medication.<sup>[104-107]</sup> Motoric slowing and longer attention span for repetitive tasks are predictable responses to stimulant medications.<sup>[104-107]</sup> Another crucial difficulty with medication treatment is that although ADHD is described as a chronic illness, the effects of stimulant medications on symptom suppression have not been shown to persist beyond the period of medication treatment, and there is no evidence that the medications promote or cause psychologic, social, or emotional growth.<sup>[68,108,109]</sup>

Not all therapeutic trials "work," however, for the reasons discussed above. Children who demonstrate dysphoria or outbursts or limited response to a medication trial are sometimes thought to need a higher dose of stimulant, a different stimulant, or a second medication; in this concerning situation, many, but not all, primary providers would ultimately refer the child to a mental health specialist. In addition, although the potential bodily side effects of stimulants, including appetite suppression and sleep disturbance, are well known and usually monitored, the mental and emotional side effects are less discussed and are not considered an indication to discontinue medication. In its practice parameter, the American Academy of Child and Adolescent Psychiatry includes in its list of "minor (expected, tolerable)" stimulant side effects mild anxiety, mild depression, mild irritability, dull/tired/listless, mild picking at skin/nail biting, and fleeting tics.<sup>[3]</sup> Whether these side effects are tolerable to the child is not known; studies that evaluate this question have not been performed. The point is that a "diagnostic trial of stimulant medication" is not necessarily straightforward, diagnostic, or benign. Interestingly, in the MTA trial, parents whose children received "behavioral therapy" were significantly more satisfied than those whose children received medication alone or medication plus "behavioral therapy."<sup>[68]</sup> Trials examining the role or efficacy of supportive psychotherapy for ADHD symptoms, compared with medications and/or behavioral therapy, are not available, and the short- and long-term effects of such an approach would be interesting.

Finally, the question of extending the diagnosis of ADHD to children ages 3 to 7 years has been broached, and medication trials are proceeding, specifically the Preschool ADHD Treatment Study, funded by the National Institute of Mental Health, which has enrolled children ages 3 to 5 years.<sup>[110]</sup> The diagnostic uncertainties of extending a criterion-based diagnosis for school-aged children to preschoolers have been reviewed.<sup>[4,111-114]</sup> The American Academy of Child and Adolescent Psychiatry practice parameter states that preschoolers are "best identified when the child is asked to do sedentary tasks requiring sustained attention in a structured classroom setting, a situation not often experienced by preschoolers."<sup>[4]</sup> In fact, many 3-year-olds have not had previous preschool experience, and the ability to behave acceptably and pay attention is influenced by many factors, including separation reactions, the nature of the tasks, the expertise of the preschool staff, and the quality of the preschool setting. The effect of longer hours of out-of-home care at an earlier age, including increased expectations for children to "behave" in such settings in the absence of their parent or primary caregiver, might be a factor in the expression of symptoms, including the ability to attend and focus in younger children. Gorski noted that "the symptoms [of ADHD] are common characteristics of all very young children."<sup>[112]</sup> Many parents can appreciate that "attentive" for a 10-year-old is completely different than for a 4-year-old, but differences in attention and expectations for attention differ fundamentally between grade-school children and preschoolers owing to their different stages of personality development and brain maturation, and for good reasons, the *DSM-IV* criteria for ADHD have not been extended per se to preschoolers.<sup>[115,116]</sup> Many teachers and child care providers "on the front lines" suspect that what they are seeing in "diagnosed" preschoolers is not a disease but developmentally shaped reactions to stress, instability, violence, bereavement, neglect, and other family and home pathology.<sup>[110,116,117]</sup> In fact, the rates of parental and home psychopathology for preschoolers diagnosed with ADHD are extraordinarily high.<sup>[30,69]</sup>

Although use of stimulant medications in toddlers and preschoolers continues to rise, there are just six controlled trials involving approximately 200 subjects total that have examined this subject. The limited data available suggest that younger children require higher doses of medication for a behavioral response and have a significantly higher rate of side effects than school-aged children and that these side effects can limit the acceptability of treatment.<sup>[118-121]</sup> Many psychiatrists are reluctant to prescribe stimulants for preschoolers owing to their unknown effect on the developing brain and personality and would intervene with traditional parent-child relationship-based therapeutic interventions for preschoolers with extreme behavioral difficulties in whom the question of an ADHD diagnosis is raised.

In conclusion, after careful review of the evidence available, it is not obvious that ADHD is either a disease or a neurobehavioral condition. ADHD is a collection of symptoms, namely, inattention, impulsivity, and overactivity, that overlaps with other major and minor mental health conditions. No diagnostic test confirms the diagnosis of ADHD, and no investigative study has identified an etiology for ADHD. Screening tools and diagnostic criteria are not validated. Although the American Academy of Pediatrics guidelines encourage primary care providers to diagnose and treat this condition, few providers will be able to identify or appropriately manage the multiple and significant comorbid disorders associated with the core symptoms called ADHD. There are extraordinary societal and financial pressures that lead to the diagnosis of ADHD and the use of stimulant medications in school-aged

children with behavioral difficulties. These include (1) inadequate availability and funding of both mental health services and educational testing resources, (2) a change in 1991 that led to the inclusion of ADHD as a reimbursable diagnosis for educational disability services under the Individuals with Disabilities Educational Act, (3) a strong marketing effort by the pharmaceutical industry for use of stimulant medications (eg, the funding of Children with Attention Deficit Disorder [CHADD], a parent support group for ADHD), and (4) economic pressures on families for both parents to work longer hours, leaving less time for approaches that require "talking therapy," making a "quick fix" involving medication and "med checks" more desirable.

Every child deserves to be cared for as an individual. Prudent and thoughtful evaluation of symptoms, including educational, psychiatric, or psychologic, and family assessment begin the process of understanding the individual child's difficulties and needs and of deciding which interventions will be most helpful to the child. Children deserve our "best shot" even in the face of resource scarcity, not a "one size fits all" approach. Certainly, many practitioners might disagree with this minority viewpoint, but the care of children can only benefit, one hopes, from transparent dialogue about challenging clinical problems.

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