The Diagnosis and Management of Attention-Deficit/Hyperactivity Disorder in Preschool Children: The State of Our Knowledge and Practice

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Jamie is a 3-year-old who is described by his parents as "always in motion." He does not sit still for more than a few minutes and seems to move from one activity to another all day long. His parents complain that he does not want to look at books when they try to read aloud to him and just wants to turn the pages without paying attention to the pictures or the story. Jamie constantly talks and interrupts others, and according to his parents, he "drives everyone crazy." Maria is 2½. Her mother dreads going to the supermarket with her because Maria grabs at all the items in the store, frequently causing a "scene," and not infrequently hurting herself. In fact, Maria has already been to the hospital emergency room on three occasions for injuring herself due to her uncontrollable behavior. Tyrell is 4 years old and has been expelled from his preschool for disruptive behavior, not listening to the teacher, and hitting other children. None of the other children in the neighborhood want to play with him. Jamie's, Maria's, and Tyrell's parents worry that their children have Attention-Deficit/Hyperactivity Disorder (ADHD) and have sought advice from their pediatrician. The pediatrician is concerned about making the diagnosis of ADHD in children of such a young age. How can she distinguish between the inattention, exuberance, and impulsivity that is part of the normal development of preschool-aged children and behaviors that represent pathologic symptomatology? Perhaps these behaviors are due to poor parenting or to poor parental coping with a temperamentally active child. Even if ADHD is diagnosed, what interventions are available or effective? When, if ever, would it be appropriate to prescribe stimulant medication? These are questions that pediatricians are frequently faced with. This article will review what is known about ADHD in preschool children, including issues related to etiology, diagnosis, prevalence, comorbidities, psychosocial and academic impairment, continuity with school-aged ADHD, and therapy.

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Etiology

Genetics and Neurobiology

There is strong evidence that ADHD and related traits (hyperactivity and inattention) are highly heritable. Studies of families and siblings have shown that parents and siblings of children with ADHD have a two- to eightfold increase in risk for ADHD.[1] Numerous twin studies have estimated the heritability of ADHD. These studies indicate that about 75 to 80% of the etiology of ADHD can be explained by genetics.[2] Adoption studies have also supported the large genetic component in the etiology of ADHD. In a study by Sprich and colleagues, while adoptive parents and siblings of ADHD children had low rates of ADHD (6 to 8%) that were not different from a comparison sample, biological parents and siblings had rates of ADHD of 18 and 31%, respectively.[3]

In contrast to the large number of genetic studies of ADHD in school-aged children, only a few studies look at preschool children. In one twin study, hyperactivity was defined as greater than the 95th percentile on the Child Behavior Checklist/2-3[4] for symptoms of hyperactivity or inattention. The results of this study estimated the heritability of hyperactive/inattentive behavior to be 70% in 3-year-olds and found a remarkably similar heritability at ages 7, 10, and 12

years.[5] Another twin study looking at hyperactive behavior in 2- ,3-, and 4-year-olds showed heritability rates of 70 to 80%.[6] Thus there is good evidence that hyperactive/inattention behavior in young children, similar to ADHD symptomatology in older children, is highly heritable.

Molecular genetic studies have implicated the D4 dopamine receptor (DRD4) gene and the dopamine transporter (DAT) gene in the etiology of ADHD in school-age children.[7] The D4 dopamine receptor is primarily found in areas of the brain involved with cognition and emotion, and there is evidence that these receptors play important roles in attention, motivation, and exploratory behavior. The DAT is the site of action for psychostimulant drugs used to treat ADHD. Therefore both of these genes have a physiologic connection to the neurobiology of ADHD. Several studies have implicated these genes in hyperactive-impulsive behavior in preschool children,[8,9] demonstrating a continuity of genetic factors from younger to older children. Nevertheless, ADHD is a complex disorder, and research concerning these genes is in a preliminary phase. It is likely that other genes will also be identified.

Environmental Factors

Despite the strong evidence for heritability of ADHD, there is a significant role for environmental factors. Twin studies are likely to overestimate heritability. Their results are usually based on report of ADHD symptoms from a parent, who is likely to know that the twins are identical or fraternal.[10] In addition, while genetic etiology may be "necessary" for the diagnosis of ADHD, it may not be "sufficient." Additional environmental factors could be critical. It is also unclear whether environmental factors may be unique causes of ADHD, or whether they always act as a "second hit" to a genetically predisposed individual.[11] Environmental factors implicated in ADHD include biologic factors (such as prenatal and perinatal factors and chemical toxins) and family and psychosocial stressors.

Biologic Factors. Mothers of children with ADHD are more likely than others to have complications of pregnancy, including toxemia and lengthy labor.[10] Prematurity or small for gestational age are also associated with attentional problems in the child.[12] These factors, through hypoxemia and hypoperfusion, may directly affect the developing brain, as has been suggested by Lou.[13] Low neonatal cerebral blood flow in preterm neonates has been shown to be associated with increased dopamine receptor availability in these same children during their adolescence in association with the diagnosis of ADHD.[14]

Thapar and colleagues studied families with twins and found that maternal smoking during pregnancy was associated with ADHD symptoms in the child. This effect was in addition to the genetic effects, and nonshared environmental influences on the diagnosis of ADHD.[15] Animal studies suggest that prenatal exposure to nicotine may affect neural development and neurotransmitters, causing an increase in brain nicotinic receptors.[16] Since nicotinic receptors are involved in dopamine regulation, there is a theoretical connection between maternal smoking and ADHD symptoms in the child. We also know that mothers who smoke have more complications of pregnancy and a higher frequency of low-birth-weight infants. They may predispose their fetuses to increased risk for hypoxemia. Thus, there are many other pathways, in addition to increased brain nicotinic receptors, through which maternal smoking may cause ADHD symptomatology.[16] These results, however, must be viewed in the context of the magnitude of the association, since only 1% of variance of ADHD symptomatology was due to maternal smoking (as compared to 73% due to genetic factors and 26% due to nonshared environmental factors).[15]

Toxicity due to environmental lead has been shown to be associated with learning and attention deficits in children 7 to 11 years of age.[17] Mendelsohn and colleagues studied 12- to 36-month-old children and found significant correlations of low-level lead exposure (blood lead between 10 and 24.9 μg/dL) with hyperactive-distractible behavior. This association persisted even after controlling for possible confounders.[18] Thus, there appears to be an association of exposure to environmental lead, even at low levels, with hyperactive and distractible behavior in very young children. As was the case with the effects of maternal smoking, the effects of lead exposure are small.

Konofal and colleagues showed that iron deficiency, as defined by low serum ferritin levels, was associated with ADHD diagnosis in a case-control study design.[19] In addition, within the ADHD group, serum ferritin levels were inversely correlated with the severity of ADHD, accounting for about 10% of the variance in ADHD severity. Since brain iron levels affect dopamine neurotransmission, there is a plausi-

ble biological mechanism for this association.[20] Although this study of children aged 4 to 14 years did not specifically focus on preschool children, iron deficiency is a problem that primarily affects young children. Therefore, we would anticipate effects of iron deficiency in the preschool age group. The causal direction of the association between iron deficiency and ADHD symptoms demonstrated in this study cannot be assumed. While there was no evidence of malnutrition in the ADHD group, it is possible that the lower ferritin levels were a marker for poorer nutritional status in this group. In that case, ADHD might cause iron deficiency rather than the reverse.

There is strong evidence that snoring, sleep-disordered breathing, and obstructive sleep apnea are associated with hyperactive and inattentive behavior and with the diagnosis of ADHD.[21] These findings have been well-documented in 4- to 5-year-olds as well as older children.[22] While up to one-third of children with frequent and loud snoring or sleep-disordered breathing will display symptoms of hyperactivity and inattention,[22] only 5% of children with ADHD are found to have obstructive sleep apnea.[21] The relationship of ADHD and sleep is further complicated by the higher incidence of general sleep disturbances in children with ADHD. It seems prudent for the clinician to take a thorough sleep history in children presenting with symptoms of ADHD and evaluate those children with snoring and sleep-disordered breathing for obstructive sleep apnea.

Psychosocial Factors. There is conflicting evidence about the relationship of psychosocial and family stressors and ADHD. There is an association of maternal depression and ADHD in preschool children[23] and there is a reported association of psychosocial adversity and ADHD symptom severity.[10] There is also evidence that preschool children who have ADHD associated with disruptive behavior problems also have more family dysfunction and parents with poorer parenting skills.[23] Nevertheless the directional, or more likely transactional, relationship between ADHD, disruptive behavior, and parenting competence is complex. It is likely that psychosocial stressors and lower parenting competence are nonspecific triggers of an underlying disorder, or are modifiers of the disorder, rather than true causes of ADHD.[10,16] As such they may be the stressors that lead a genetically susceptible individual to a full-blown diagnosis, or they may lead to worsening of symptoms and a range of comorbid psychopathologies.

There has been concern that excessive television viewing, especially occurring at an early age, may shorten a child's attention span and lead to symptoms of ADHD. Christakis and colleagues used the National Longitudinal Survey of Youth to assess the relationship of early television viewing at ages 1 and 3 with hyperactivity and attentional problems at age 7.[24] They found a significant relationship between the number of hours of television viewed and risk of attentional and hyperactive problems. Although the odds ratios were statistically significant, they were only slightly greater than one. In view of potential confounding, such a weak relationship is not strongly supportive of a causative role for television viewing.

Summary. ADHD has a strong genetic causative basis, accounting for approximately 75% of its diagnosis. Nevertheless, there are a number of biologic and psychosocial factors that may play a deciding role in either triggering an underlying predisposition, or in modifying the severity of symptomatology. Although most studies of etiology have looked at school-aged children with ADHD, there are a number of studies that have focused on the etiology of ADHD in preschool children or on the determination of ADHD risk factors occurring early in life. In addition, most of the biologic and psychosocial risk factors are present in either the prenatal period, the perinatal period, or early childhood and are likely to be implicated in the etiology of ADHD diagnosed in preschool children.

Diagnosis and Prevalence

Concerns About Use of DSM-IV Criteria in Diagnosis of ADHD in Preschool Children

The diagnosis of ADHD is generally made based on the child meeting the criteria delineated in *Diagnostic and Statistical Manual of Mental Health Disorders Fourth Edition Text Revision* (DSM-IV-TR).[25] The DSM-IV criteria describe three subtypes of ADHD: inattentive, hyperactive-impulsive, and combined. For the inattentive and hyperactive-impulsive subtypes, children must have at least six of nine symptoms in the respective subtype. For the combined subtype, the child must meet criteria for both the inattentive and the hyperactive impulsive subtypes. See Table 1 for a list of symptoms. These symptoms must occur "often," not occasionally, and persist for at least 6 months. Importantly, they must be severe enough to be "maladaptive and inconsistent with developmental level"

TABLE 1. DSM-IV-TR symptoms of ADHD[25]

Symptoms of inattention (occurring often)
1. Fails to give close attention to details, makes careless mistakes
2. Has difficulty sustaining attention
3. Does not seem to listen when spoken to
4. Does not follow through on instructions or finish schoolwork or chores
5. Has difficulty organizing tasks and activities
6. Avoids or dislikes to engage in tasks that require sustained mental effort (eg, schoolwork or homework)
7. Loses things
8. Distracted by extraneous stimuli
9. Forgetful in daily activities
Symptoms of hyperactivity-impulsivity (occurring often)
Hyperactivity
1. Fidgets with hands or feet or squirms in seat
2. Leaves seat in classroom or in other situations where expected to remain seated
3. Often runs about or climbs excessively in situation where it is inappropriate
4. Difficulty playing quietly
5. "On the go" or acts as if "driven by a motor"
6. Talks excessively
Impulsivity
7. Blurts out answers before questions completed
8. Difficulty awaiting turn
9. Interrupts or intrudes on others (eg, in conversations or games)

and some symptomatology must be present prior to 7 years of age. Impairment from the symptoms should exist in two or more settings (eg, school and home), and significant impairment should be evident in social, academic, or occupational domains.

DSM-IV-TR does not specify a lower limit of age for diagnosis, and, as stated, *requires* symptoms prior to 7 years of age. Prospective studies indicate that peak age of onset of ADHD is between 3 and 4 years of age.[26] In a referred sample of school-aged children with diagnosed ADHD, mothers reported that onset of symptoms occurred at or before the fourth birthday in two-thirds of the children.[27] Therefore, it is likely that children in the preschool age group, defined as 2 through 5 years of age, will come to the attention of clinicians because of ADHD symptomatology. However, less is known about the use of DSM-IV criteria for diagnosis of ADHD in preschool children than in school-age children.[28] Since the DSM-IV criteria for diagnosis of ADHD are the same regardless of the age of the child, the developmental progression of normal behaviors and the differentiation of abnormal symptoms from normal age-appropriate behaviors is not addressed in DSM-IV-TR. The only guidance given in DSM-IV-TR concerning differentiating normal developmentally appropriate behavior from abnormal behavior is that the symptoms should be "inconsistent with developmental level" in order to be scored positively.[25] DSM-IV-TR states that it is "difficult to establish this diagnosis in children younger than age 4 or 5 years, because their characteristic behavior is much more variable than that of older children and may include features that are similar to symptoms of Attention-Deficit/Hyperactivity Disorder."[25] It is left to the clinician to determine whether the observed or reported behaviors (high activity level, short attention span, need for immediate gratification, impulsivity, opposition to parental request) are developmentally appropriate for the young child or representative of clinical pathology. The potential inability of the clinician to appreciate that many of the DSM-IV symptoms may be normal for younger children could lead to overdiagnosis of ADHD in this age group.

Another concern about the use of DSM-IV in preschool children is raised by the skewed distribution of children who met the criteria for the hyperactive-impulsive subtype in the DSM-IV field trials.[29] Only 24% of children categorized as hyperactive-impulsive subtype were older than 6 years, whereas more than 70% of children categorized as inattentive subtype or combined subtype were older than 6 years. Lahey and colleagues have suggested two possible explanations for this skewed distribution,[30] as follows: (1) Few older children are found with the hyperactive-impulsive subtype because as children grow older they exhibit more symptoms of inattention as the demands on them for attention increase (increased schoolwork and homework, tasks requiring greater concentration). Therefore younger children who were categorized as hyperactive-impulsive may be categorized as combined subtype at older ages. (2) Younger children categorized as hyperactive-impulsive are inappropriately diagnosed as ADHD because they exhibit a variation of normal activity and exuberance. As they mature, they no longer meet the criteria for any subtype of ADHD.

A third concern about using DSM-IV criteria in preschool children is the wording of the descriptions of a number of the symptoms.[31,32] Phrases such as "fails to finish schoolwork, chores, or duties in the workplace" and "often leaves seat in classroom" seem inappropriate to describe the activities and behaviors of preschool children. The lack of developmentally appropriate examples of behavior in the DSM-IV

criteria make the diagnosis of ADHD in preschoolers problematic. The existing examples may be confusing to parents and teachers and lead to a lack of reliability in their reports. Even worse, they may lead to overdiagnosis of ADHD in the preschool child.

Reliability of ADHD-Specific Rating Scales in Preschool Children

ADHD-specific rating scales are recommended for use in school-age children to aid the clinician in diagnosing and managing symptoms and impairment due to ADHD.[33] These rating scales come in separate forms for parent and teacher and have been shown to be reliable and to accurately distinguish children with ADHD from children without ADHD in the school-age group.[34] Most of these rating scales are now based directly on the 18 symptoms listed in the DSM-IV-TR and include a Likert scale scoring system for frequency of symptoms from 0 to 3 (0 = never, seldom; 1 = occasionally; 2 = often; 3 = very often).

Several of the ADHD-specific rating scales have been shown to be reliable when used with preschool children 3 years and older. These include the Connors Parent Rating Scale–Revised, the Connors Teacher Scale–Revised[35,36] (validated on children 3 years and older), and the AD/HD Rating Scale–IV parent and teacher versions.[37] For example, the Conners' Parent Rating Scale–Revised has been shown to have moderate to high test-retest reliability in diagnosing the three ADHD subtypes with reliability coefficients ranging from 0.67 to 0.81 for the DSM-IV subscales. Cronbach's alpha coefficients, a measure of internal consistency, have been measured for both parent and teacher versions of the Conners' Rating Scales–Revised and range from 0.82 to 0.96 for the DSM-IV subscales.

The Early Childhood Inventory-4 (ECI-4) parent and teacher versions[38,39] is also based on the DSM-IV and has subscales for ADHD inattention and hyperactive-impulsive subtypes. The ECI-4 ADHD subscales, used for children 3 to 5 years of age, have been shown to have moderate to high test-retest reliability in diagnosing the three ADHD subtypes with Pearson *r*'s ranging from 0.64 to 0.72. Cronbach's alpha coefficients have been measured for the ADHD subscales on both the parent and the teacher versions of the ECI-4 and are consistently over 0.80. The ECI-4 subscales for ADHD are the same as the ADHD subscales on the ADHD Symptom Checklist-4[40] and therefore this rating scale, specific to ADHD, can also be considered to be reliable for children 3 to 5 years old. Several other commonly used ADHD-specific rating scales, the Vanderbilt,[41-43] which comes with the American Academy of Pediatrics ADHD Toolkit,[44] and the SNAP-IV,[45,46] have no reported psychometric data on their use with young children. Nevertheless, their content and structure are so similar to the rating scales for which there is reliability data that it is likely that their use with preschool children would also be reliable.

The Child Behavior Checklist for Ages 1½ to 5, a broad checklist for behavioral symptoms in young children, has two subscales that pertain to ADHD symptoms.[4] The Attention Problems subscale and the DSM-oriented Attention Deficit/Hyperactivity Problems subscale have reported test-retest reliability coefficients ranging from 0.74 to 0.78. Since the CBCL has 100 items, only 6 of which pertain to ADHD, it cannot be recommended for specific diagnosis or management of ADHD.

The Preschool Age Psychiatric Assessment (PAPA) is a structured parent interview assessing psychiatric symptoms and disorders in preschool children.[47] In studies of its test-retest reliability, the kappa for the diagnosis of ADHD was 0.74 and the intraclass correlation coefficient for the test-retest reliability of the ADHD scale score was 0.80.[48] The PAPA takes approximately 2.5 hours to perform and score, so it is appropriate for in-depth psychiatric diagnosis and research, but not for pediatric office screening or assessment of ADHD.

In summary, ADHD-specific rating scales, subscales on behavioral checklists, and structured psychiatric parent interviews have all been shown to be reliable in assessing preschool children for ADHD. Despite concern about applicability and wording of DSM-IV ADHD symptom criteria for preschool children, tools for the reliable measurement of ADHD symptoms in preschool children are available to the clinician.

Prevalence of ADHD in School-Aged and Preschool Children

Prevalence rates of ADHD in school-aged children vary in study samples from 4 to 12% (median 5.8%), with prevalence rates higher in community samples (mean 10.3%) than in school samples (mean 6.9%).[34] These studies varied as to whether they required documentation of impairment for the diagnosis of

ADHD, as indicated in DSM-IV. Most of these studies were based on previous DSM criteria (DSM-III and DSM-III-R), neither of which required documented impairment in social or academic functioning, or evidence of impairment in both school and home. In these school-aged samples, the male/female ratio of prevalence is approximately 3:1. In a school-based study of children in kindergarten through fifth grade using teacher assessment (including a measure of impairment), Wolraich and colleagues found that 48% of the children with ADHD had the inattentive subtype, 43% had the combined subtype, and only 9% had the hyperactive-impulsive subtype.[42]

A high proportion of school-aged children with ADHD have comorbid conditions, specifically oppositional defiant disorder (ODD), conduct disorder (CD), depressive and anxiety disorders. ODD involves a pattern of negativistic, defiant, and hostile behavior lasting for at least 6 months. Children with ODD argue with adults, refuse to comply with adults' requests or rules, and are often angry, touchy, and annoying to others.[25] In contrast, CD is a persistent pattern of behavior in which the basic rights of others and age-appropriate societal norms are violated. Children with CD may be aggressive to people and animals, destroy property, lie, and steal.[25] Mean prevalence rates for these comorbidities in school-aged children with ADHD are highest for ODD (35%), with CD and depression occurring in about 25% of these children. Anxiety disorders are least common, with mean prevalence rate of 18%.[34] In a recent survey of British children and adolescents, 53% with ADHD had a comorbidity of another disruptive behavior disorder, including 27% with ODD, and 18% with CD.[49] Less is known about prevalence rates for co-occurring learning disabilities or learning problems, although much of the impairment in school-aged children is related to poor academic performance. In a school-based study,[50] over 60% of children with ADHD had academic problems, with a differential pattern among subtypes. Almost 75% of children with inattentive or combined subtypes had academic problems, while only 23% of children with the hyperactive-impulsive subtype had academic problems. However, diagnosis of a separate, but comorbid, learning disability (versus identification of learning problems directly related to ADHD symptoms and behaviors) is often difficult. There is also the problem of definition. Perhaps inattentive symptoms of ADHD are a specific learning disability, albeit not defined in the DSM-IV-TR.

In the last 10 years, a number of studies have attempted to address the issue of prevalence of ADHD in US preschool children. Studies that come from referral or psychiatric clinic populations reflect sampling biases and cannot provide valid estimates of rates of ADHD in the general population. This review, therefore, only considers studies that have community, school, or primary care samples.[40,48,51-54] Table 2 summarizes the results of these studies. All studies are based on parent report, not parent *and* teacher report, and therefore do not necessarily address finding impairment due to symptoms in at least two settings. None of the studies using symptom checklists assess impairment in social, academic, or family functioning. We know that when a measure of impairment is required for the diagnosis of ADHD, in addition to DSM-IV symptom criteria as measured by a symptom checklist, reported prevalence rates drop substantially. In the study of school children by Wolraich and colleagues, when DSM-IV impairment criteria were not considered, 16% of the sample was diagnosed with ADHD. When DSM-IV impairment criteria were required for diagnosis of ADHD, overall prevalence of ADHD dropped to 6.8%.[42] Several of the studies of preschool prevalence also have substantial refusal rates or uncontrolled selection of patients, raising the concern of selection bias. Finally, none of the checklist studies, nor DSM-III-R-based studies, require that symptoms are long lasting (ie, at least for the last 6 months). All of these factors (the lack of teacher report, the lack of DSM-IV impairment criteria in some studies, the potential for selection bias, and the potential for mistakenly diagnosing a transient problem as a chronic disorder) may lead to falsely elevated estimates of prevalence rates.

The overall prevalence rate of the ADHD in these studies of preschool children, calculated by weighting the rates in individual studies by sample size, was 4.9% (see Table 2). However, considering only those studies that required a measure of impairment for diagnosis decreases the prevalence rate to 2.8%.[48,51,52] Considering only those studies that used DSM-IV criteria for diagnosis increases the prevalence rate to 6.3%.[40,48,53,54] It is possible that studies using DSM-IV criteria, with a separate subtype for hyperactive-impulsive symptoms, may lead to higher prevalence rates in preschool children than those studies using DSM-III-R criteria. In the DSM-IV field trials, there was a 15% increase in diagnosis of ADHD, all subtypes and all ages, when using DSM-IV criteria

TABLE 2. Prevalence of preschool ADHD (parent as informant)

Study	Measure	Impairment measured?	Child's age (yrs)	Ratio boys/girls with ADHD	ADHD-I (%)	ADHD-HI (%)	ADHD-combined (%)	ADHD total (%)
Lavigne et al (1996)[51]	Consensus evaluation (two psychologists); DSM-III-R	Yes	2–5	2:1	N/A	N/A	N/A	2.0
Gadow and Sprafkin (1997)[40]	DSM-IV checklist (ADHD subscales)[a]	No	3–5	1.5:1	0.0	3.1	2.5	5.7
Keenan et al (1997)[52]	Structured Diagnostic DSM-III-R Interview (K-SADS)[b]	Yes	4.6–5.8	N/A	N/A	N/A	N/A	5.7
Gimpel and Kuhn (2000)[53]	DSM-IV checklist for ADHD[c]	No	2–6	2:1	2.0	3.6	4.0	9.5
Gadow et al (2001)[54]	DSM-IV checklist (ADHD subscales)[a]	No	3–5	2:1	0.9	3.6	1.5	6.0
Egger et al (in press)[48]	Structured Diagnostic DSM-IV Interview (PAPA)[d]	Yes	2–5	2.5:1	0.0	1.8	1.5	3.3
Weighted average prevalence[e]					0.8	3.1	2.4	4.9[f]

[a]Early Childhood Inventory-4 (ECI-4).[38]
[b]Kiddie-Schedule for Affective Disorders and Schizophrenia.[55]
[c]AD/HD Rating Scale-1.[37]
[d]Preschool Age Psychiatric Assessment.[47]
[e]In each subtype and in total ADHD prevalence, all applicable studies were used in weighted average calculation.
[f]If only studies with clinical diagnostic methods/impairment measures included in analysis, total ADHD prevalence = 2.8%. If only studies with DSM-IV criteria included in analysis, total ADHD prevalence = 6.3%.

compared to previous DSM criteria.[29] There was also an increase in diagnosis of children in the preschool age group, primarily due to diagnosis of the hyperactive-impulsive subtype. However, all of the DSM-IV-based prevalence studies listed in Table 2 except for one[48] used symptom checklists and thus did not include a measure of impairment. The one DSM-IV-based study that did require impairment for the diagnosis of ADHD found a prevalence rate of 3.3%.[48] Lack of measurement of impairment, therefore, seems to be the major factor causing higher prevalence rates in the DSM-IV group of studies. The overall prevalence rate of 4.9% (2.8 to 6.3%) is similar to the prevalence rates found for US school-aged children (5.8%).

As mentioned at the beginning of this section, the distribution of ADHD subtypes in preschool children is markedly different from the distribution in school-aged children (Table 3). The prevalence of the inattentive and hyperactive-impulsive subtypes is reversed, with few children in the preschool age group meeting criteria for the inattentive subtype and few children in the school-aged group meeting criteria for the hyperactive-impulsive subtype. These data are consistent with the findings in the original DSM-IV field trials[29] and with results of studies of preschool children based on teacher, not parent, report.[56]

TABLE 3. Comparison of ADHD subtypes in preschool and school-aged children

ADHD subtype	Preschool (% total prevalence)[a]	School-aged (% of total prevalence)[b]
Inattentive	13	48
Hyperactive-impulsive	49	9
Combined	38	43

[a]Based on weighted average prevalence in studies of ADHD in preschool children (see Table 1).
[b]Wolraich et al 1998.[42]

Despite the reversal of the prevalence of these two subtypes from the preschool to the school-age periods, the similar total prevalence of ADHD among preschool children as compared to school-aged children is generally reassuring. If the DSM-IV criteria were invalid for use with preschool children and led to overdiagnosis of ADHD (primarily due to the inability to differentiate normal activity and lack of impulse control in this age group from pathology), prevalence rates in preschool children would be falsely elevated and would be higher than those in school-aged children. In view of the reported prevalence rates of ADHD in preschool children, it is, therefore, less

likely that the reversal of subtypes is due to overdiagnosis, and more likely that other factors explain these differences. One explanation is that offered by Lahey and colleagues.[30] As noted previously, they suggested that, as children get older, the increased demands for attention would change their categorization from the hyperactive-impulsive subtype to the combined subtype. Egger and colleague's finding that the combined subtype is nonexistent in 2-year-olds diagnosed with ADHD, and its prevalence increases dramatically from age 3 to 5, is consistent with this hypothesis.[48] Another possible explanation for the observed differences in subtype prevalence is that while some of the younger children who were categorized as hyperactive-impulsive as young children no longer meet criteria for hyperactive-impulsive behavior as they mature, they now exhibit symptoms of inattention as the demands for attention increase. Their attentional difficulties become apparent and more easily diagnosed.

Gender differences in preschool children seem less pronounced than in older children. In contrast to a 3:1 ratio of boys to girls in school-aged children, the ratio of boys to girls diagnosed with ADHD in the preschool age group is 2:1 (see Table 2). Gender differences among ADHD *subtypes* in preschool children are less clear. One study reported an almost 10-fold greater prevalence of the combined subtype in boys as compared to girls.[48] Other studies found no differential prevalence rates among the three subtypes due to gender, with boys consistently exhibiting somewhat higher prevalence of ADHD symptoms among all three ADHD subtypes.[53,54]

Common Comorbidities in Preschool ADHD

Similar to school-aged children with ADHD, preschool children with ADHD are likely to have comorbid behavioral disorders. Lavigne and colleagues found that the majority (87%) of preschoolers with ADHD had comorbid disorders, almost always ODD.[51] Gadow and colleagues reported that approximately half of preschool children in a community and primary care sample who met DSM-IV cutoffs for ADHD symptoms had comorbid ODD.[54] Eggers reports that over half (55%) of preschool children with ADHD have one or more comorbidities: 39% have CD, 36% have ODD, 13% have depression, and 15% have anxiety disorders.[57] Multiple comorbidities were not uncommon, with 19% of children having two comorbidities and 12% having three morbidities. Eggers found a significant association of ADHD with all of these comorbidities except anxiety disorders; anxiety disorders were diagnosed in approximately the same number of children with or without ADHD.

Preschool children with the combined subtype of ADHD are more likely to have comorbid ODD. In a study of Swedish children 3 to 7 years of age, children with combined subtype ADHD were four times as likely to have ODD as children with the inattentive subtype and twice as likely to have comorbid ODD as children with the hyperactive-impulsive subtype.[58] Thus comorbidity with ODD is not only associated with more symptomatology due to the addition of ODD symptoms but is likely to be a marker for more severe ADHD symptomatology as well. In addition ADHD children with comorbid ODD were significantly more likely to be anxious or depressed. This study also documented the high prevalence of ODD symptoms in young children with ADHD, even when they did not meet all criteria for comorbid ODD. Ninety-two percent of the ADHD children without ODD had at least one ODD symptom. Furthermore, ADHD children without ODD scored significantly higher on an ODD rating scale than comparison children without ADHD.

In summary, preschool children with ADHD are likely to have comorbidities, especially ODD. In all studies looking at preschool children, at least half suffered from a comorbid condition. In approximately one-third of cases, two or more comorbidities are present. The addition of the diagnosis of ODD is likely to be a marker for more severe ADHD symptomatology. Even those children without the diagnosis of ODD are likely to have some oppositional behaviors.

Validity of DSM-IV Criteria for Diagnosis of ADHD in Preschool Children

The studies of the prevalence of ADHD in preschool children (which show rates similar to prevalence rates of ADHD in school-aged children) appear to indicate that using DSM-IV criteria leads to the diagnosis of ADHD in a small group of young children in need of intervention and does not lead to the overdiagnosis of ADHD in normally active, rambunctious preschoolers. However, if preschool children are in fact being correctly identified with ADHD by DSM-IV criteria, then those children should have strong evidence of psychosocial and academic impairment typical of ADHD. There should also be some evidence of a

"dose effect"; that is, as severity of symptomatology increases, severity of impairment should also increase. Furthermore, since ADHD is a chronic disease, there should be evidence of stability of both symptoms and impairment over time. As these children get older and move into the school-age period, they should remain symptomatic and impaired, and continue with the diagnosis of ADHD. Finally, the same underlying neuropsychological deficits found in school-aged children with ADHD, such as difficulties with executive functioning, delay aversion, and inhibitory control, should be found in preschool children diagnosed with ADHD. A number of studies have evaluated these issues: psychosocial and academic impairment in preschool children with ADHD; dose effect of ADHD symptoms on impairment; stability of ADHD symptoms, impairment, and diagnosis over time; and neuropsychological profile of preschool ADHD.

Psychosocial and Academic Impairment in Preschool Children with ADHD. Lahey and colleagues compared 4- to 6-year-old children with DSM-IV symptom criteria for ADHD to a group of children recruited from the same or nearby schools.[30] Comparison children were matched to the ADHD cohort on gender, ethnicity, age, and socioeconomic status. Analyses controlled for age, gender, intelligence, socioeconomic status, and comorbidities (ODD, CD, anxiety, and depression). Each subtype of ADHD was found to be associated with functional impairment in social and academic skills. This was true for the results of teacher, parent, and self-assessments of functioning, as well as standardized testing. Children with all ADHD subtypes were rated as significantly less popular with classmates than the comparison children, and those children who met criteria for the combined subtype were actively disliked. All children with ADHD were perceived by teachers to be significantly less prosocial, less cooperative, and less assertive than those in the comparison group. Children in the hyperactive-impulsive and combined subtypes were also rated as significantly more disruptive and less self-controlled than children in the comparison group. Of interest, the investigators also found that children in each of the ADHD subtypes reported significantly greater problems in friendships than children in the comparison group, corroborating the impression of their teachers. In addition, parents and interviewers rated children in each ADHD subtype lower on global ratings of adaptive functioning than the comparison group.

In this study, parents of children in the hyperactive-impulsive subtype also reported significantly more unintentional injuries caused by the child's behavior than parents of comparison children. There was a trend toward greater unintentional injuries in the combined subtype. For example 36% of children with the hyperactive-impulsive ADHD subtype had experienced unintentional injuries as compared to 12% of non-ADHD children. Children with ADHD were also found to have greater academic difficulties than children in the comparison group. Depending on subtype, 15 to 25% of the children with ADHD were in special education as compared to 0% of non-ADHD children. Children who met criteria for the combined or inattentive subtypes had significantly lower mathematics achievement relative to intelligence than comparison children. Children in the hyperactive-impulsive subtype showed a trend toward lower mathematics scores than comparison children. Furthermore, children with the inattentive subtype trended toward underachievement in reading compared to non-ADHD children.

In summary, preschool children with all ADHD subtypes were found to be significantly impaired in social and academic functioning. Similar to school-aged children with ADHD,[42,50] preschool children with combined and inattentive subtypes were more likely to experience academic difficulties, and preschool children with combined and hyperactive-impulsive subtypes were more likely to be considered disruptive and lacking self-control. Of interest was the finding of the additional morbidity of increased unintentional injuries in preschool children with the hyperactive-impulsive subtype of ADHD.

Egger and colleagues also found significant psychosocial and academic impairment in preschool children with ADHD.[48] Preschool children with ADHD, in their study of 2- to 5-year-olds, were eight times more likely to show significant impairment in relationships and functioning in the home and in school than children without ADHD. For example 71% of the children with ADHD had impaired relationships with their parents versus 12% of non-ADHD preschoolers. Ratios of impaired relationships with teachers, siblings, and peers for ADHD preschool children versus those without ADHD were 43:4, 41:10, and 50:6%, respectively. Overall, 89% of preschool children with ADHD had significant impairment in at least one social relationship.[57] Children with the combined subtype were more impaired than children with the hyperactive-impulsive subtype (no children with the

inattentive subtype were identified), and children with comorbidities such as ODD were more impaired than children with ADHD alone. Impairment was found in both home and preschool or daycare. More than half of the parents expressed serious concerns about managing their child's behavior and reported that it interfered with family activities (such as taking the child to a store or restaurant). Mothers reported that 58% of the ADHD diagnosed preschool children were unable to act appropriately in public places, as compared with 6% of non-ADHD children. Over 40% of the children with ADHD had been suspended from school or daycare compared to 0.6% of the non-ADHD preschoolers. Almost 16% of the children with ADHD had been expelled. All of those who had been expelled had the combined subtype with comorbidities.

In a study of 94 middle-class 3- to 5-year-olds, DuPaul and colleagues found that preschool children with ADHD exhibited significantly more behavior problems and were significantly less socially skilled according to behavior ratings by their teachers and parents.[59] These differences were large, with effect sizes for differences of behavior problems and social skills between ADHD and non-ADHD children greater than 1.0 and frequently in the range of 2.0 to 4.0. Effect sizes are mean differences between the groups in standard deviation units. During observations of parent–child interactions, ADHD children were more frequently noncompliant and inappropriate and their parents were more likely to respond with negative behavior toward their children. Parents of preschoolers with ADHD experienced high levels of stress and were coping less adaptively compared to parents of non-ADHD preschoolers. The ADHD preschool children also scored significantly lower on a test of developmental and pre-academic skills. On average, the ADHD group scored 1 standard deviation lower on reasoning, academic skills, and concept development than the comparison group or than the expected mean for their age. Thus, ADHD preschoolers exhibit impairment in social skills and pre-academic skills, and their relationships with their parents are negatively affected by their behavior. Their families are more stressed and experience greater family dysfunction than families of preschool children without ADHD.

There is also some evidence that young children with ADHD, especially those with inattentive symptoms (eg, combined and inattentive subtypes), have deficits in language development and emergent literacy skills. Lonigan and colleagues found significant, unique associations between inattention measured by the Conners' Teacher Rating Scale and language development and phonological processing abilities.[60] This associated impairment is an important one, since early language and emergent literacy skills are predictive of reading abilities in school.[61] Understanding causality in this association is complex. One hypothetical causal pathway is that behavior problems, especially inattention, interfere with language development and the attainment of reading skills.[62] According to the transactional model of language acquisition, children learn language through interaction with their parents. If the child's inattentive (or hyperactive-impulsive) behavior interferes with joint attention activities, parental expansion and extension of the child's language may be ineffective. Similarly, if the child is inattentive to reading aloud activities, acquisition of prereading skills and beginning phonological processing may be disrupted. The child's behavior may also lead the mother to abandon language or reading activities. This direction of this causal pathway is supported by research that shows that attention problems in kindergarten predict later reading difficulty, whereas early poor reading did not predict later inattention.[63] Another possibility is that the process of learning language, in which the parent directs the child's attention to conversations, objects, and concepts, is important in the development of memory, executive processing, and self-regulation.[64] If this process does not occur due to parental dysfunction or the child's innate language problems, then the development of attention and executive functioning may be impaired. Furthermore, poor language skills and other learning difficulties may frustrate the preschool child, leading to inattentive, hyperactive, and disruptive behaviors. In one study of low socioeconomic status preschool boys, emergent reading skills, attention, and disruptive behaviors were measured.[65] Path analysis in this sample seemed to indicate that poor emergent reading skills (eg, receptive and expressive language and letter recognition) may make it difficult for the child to pay attention in the classroom and secondarily lead to disruptive behavior. Of course, the causal pathways may be bidirectional. Problems with attention may lead to poor language and pre-academic skills; poor language and pre-academic skills may worsen difficulties with attention and behavior. Finally, common genetic influences may cause both inattention and language/reading difficulties, leading to their associa-

tion as comorbidities.[66] Further research is needed to elucidate which of these causal pathways is most important.

Dose Effect of ADHD Symptoms on Impairment in Preschool Children. DSM-IV criteria were developed with strict cutoffs for diagnosis, with a requirement for each of the subtypes of six or more symptoms occurring "often."[25] The behaviors of inattention, hyperactivity, and impulsivity that parents and teachers report, however, appear to follow a normal distribution rather than a bimodal one.[67] The cutoff of six or more symptoms in the DSM-IV was somewhat arbitrary and partly based on being conservative in labeling children with ADHD, as well as opting for consistency among the number of symptoms required for each of the subtypes.[29] In addition, some of the ADHD checklist scales use normative data and define ADHD as scores lying greater than 1.5 or 2 standard deviations above the mean.[36] It is therefore difficult to draw the line between normality and disorder. The DSM-IV field trials found a linear relationship between number of hyperactive-impulsive symptoms and impairment as measured by the children's global assessment scale, demonstrating a "dose effect" between number of symptoms and level of impairment.[29] One would expect, therefore, that a dose effect for increasing number of symptoms causing increasing impairment could be demonstrated in preschool children, if the measurement of symptoms by DSM-IV criteria in those children is valid.

In the PAPA test-retest study, a dose effect was, in fact, demonstrated.[48] A linear relationship was found between number of symptoms and level of impairment. For each additional inattentive symptom or hyperactive symptom, the child's probability of being impaired nearly doubled with an odds ratio of 1.7. For example, with three hyperactive impulsive symptoms, 31% of the children were impaired; with four hyperactive-impulsive symptoms, 57% of children were impaired.[57] This demonstrated dose effect supports the construct validity of ADHD in preschool children, since it is consistent with our understanding of ADHD in school-aged children.

Stability of ADHD Symptoms, Impairment, and Diagnosis from the Preschool to School-Age Period. It is particularly important to evaluate the stability of ADHD symptomatology and impairment in preschool children. The thorny issues of behavioral and drug treatment for these children make it essential to know if these symptoms and impairment persist or are transient.

Several studies have looked at the persistence of symptoms of hyperactivity as reported by mothers. Campbell and colleagues identified a cohort of 2- to 3-year-olds with problem behaviors including hyperactivity and difficult management by mothers and teachers. At follow-up at age 6, about one-third met DSM-III criteria with attention deficit disorder (ADD), and 50% had ADD, aggressive behavior, or both.[68] Two-thirds of the children diagnosed with a DSM-III externalizing disorder (ADD, ODD, or CD) at 6 years of age persisted with a DSM-III externalizing disorder at age 9.[69]

Similar results were found in another long-term follow-up study of hyperactive preschool children.[70] In this study, the preschoolers with hyperactivity were identified as having greater impairments in language skills than comparison children. Over a 12-year follow-up period, they persisted in having poorer cognitive skills, lower levels of reading ability, as well as continued disruptive and inattentive behaviors and higher rates of DSM-III disorders.

In a third study, investigators followed an economically disadvantaged group of 4.5- to 5-year-olds identified as "acting out" in preschool through the third grade. Eighty percent of the acting out children were considered to have persistent behavior problems in at least two of three grades.[71] In addition to persistent behavior problems, the acting out preschoolers had significantly lower academic achievement in the primary grades and were viewed by their teachers as more impaired in peer relationships and in adjustment to school than comparison children. The home environment, especially degree of stimulation, predictability, and organization, was a strong protective factor, and measures of the home environment were significantly higher in the comparison group, as well as in those children in the acting out group who reverted to normal behavior during the primary grades.

There is only one study that looks at the persistence of impairment in preschool children diagnosed with ADHD by DSM-IV criteria.[72] Children 4 to 6 years of age were followed for three consecutive years and re-evaluated yearly. Ninety-six children had DSM-IV ADHD (full ADHD group); 29 children had DSM-IV symptom criteria for ADHD but met criteria only in one setting ("situational" ADHD group), and 130 children were without ADHD (comparison group). Seventy-nine percent of the full ADHD group met full

diagnostic criteria for ADHD at least twice during the 3-year follow-up period. In contrast, 35% of the situational ADHD group and 3% of the comparison group met full diagnostic criteria at least twice during the follow-up period. Social and academic impairments, documented at diagnosis, also persisted during follow-up. The full ADHD group exhibited significantly greater social, academic, and global impairments during the 3 years of follow-up than the comparison children, with the situational ADHD group experiencing an intermediate level of impairment. The stability of impairment was impressive, with kappas in the range of 0.50 to 0.79 for agreement of significant impairment in the home, in peer relations, in school, and for academic problems and social preference. Global impairment ratings by parents and interviewers were equally stable. Over 30% of the full ADHD group and 25% of the situational ADHD group were placed in special education in at least 1 of the 3 years of follow-up, as compared to less than 10% of the comparison group. Over 60% of the full ADHD group and over 50% of the situational ADHD group experienced an unintentional injury during the follow-up period, as compared to 16% of the comparison group.

In summary, ADHD diagnosed in the preschool period persists with remarkable stability and is associated with significant and persistent impairment in social and academic functioning into the elementary school grades. Preschool children identified as "normal" also remain remarkably stable and continue to be asymptomatic and unimpaired over a period of 3 years. Of interest, preschool children who do not meet full DSM-IV criteria for ADHD, but who show significant ADHD symptomatology, also continue to show significant impairment into the elementary school grades.

The Neuropsychological Profile of Preschool ADHD. School-aged children with ADHD have been shown to demonstrate a variety of neuropsychological deficits. Most of these deficits are categorized as "executive functions" associated with the frontal-striatal circuits implicated in the changes seen in neuroimaging of children with ADHD.[73] Executive functions are a set of brain functions including response inhibition, cognitive flexibility or set shifting, planning, and working memory. These neuropsychological processes have been shown to be generally impaired in school-aged children with ADHD.[74,75] In addition, ADHD school-aged children appear to be unwilling to delay their need for gratification, and given a choice between a small immediate reward and a large delayed reward, they choose the immediate reward.[76,77] While some of these deficits can be seen in children with other diagnoses (such as high functioning autism and ODD),[78] executive dysfunction and delay aversion are neuropsychological characteristics that are consistent with the diagnosis of ADHD.

Sonuga-Barke and colleagues tested a community sample of 156 children between 3 and 5.5 years of age and diagnosed a subgroup with ADHD through a structured clinical interview based on DSM-IV criteria.[79] All children were given an age-appropriate battery of tests measuring executive functions (including working memory, set shifting or cognitive flexibility, and planning) as well as measuring delay of gratification and preference for delayed rewards. Analysis of test results revealed two significant factors: executive dysfunction and delay aversion. Both these factors were predictive of the ADHD symptoms, even after controlling for IQ, age, and the presence of conduct problems.

Hughes and colleagues studied executive functioning in a group of children 3 to 5 years of age.[80] Children with ADHD-like symptoms were not diagnosed with strict DSM-IV criteria, but were rated by their mothers as above the 90th percentile for hyperactivity on a strengths and weaknesses questionnaire and were compared to a group of children who scored in the normal range. The hyperactive preschoolers scored significantly lower on tests of working memory, planning, inhibitory control, and cognitive flexibility.

The results of these studies indicate that preschool and school-aged children with the diagnosis of ADHD share similar neuropsychological characteristics. These studies provide additional support for the construct validity of preschool ADHD.

Treatment

What We Know About the Treatment of ADHD in School-Aged Children

Treatment of ADHD in school-aged children involves use of psychostimulants and behavioral interventions. Behavioral interventions have focused on parent training, behavioral modifications in the classroom, or both. Efficacy of both psychostimulant medication[81] and behavioral therapy[82] has been shown in multiple studies.

While most of the studies have looked at short-term efficacy, the NIMH Collaborative Multisite Multimodal Treatment Study of Children With Attention-Deficit/Hyperactivity Disorder (MTA) looked at these treatments with endpoints at 14 months.[83,84] The MTA study compared almost 600 children, ages 7 to 9 years, assigned to one of four treatments: medication management, behavior modification (home, school, and summer camp), a combined behavioral and medication treatment group, and a routine community treatment comparison. For ADHD symptoms, both the medication management and the combined treatment groups improved significantly more than the behavioral modification or community groups. Effect size (ES) of the improvement was large, equivalent to approximately 0.60 standard deviation units. For ADHD symptoms, no significant advantage was found for adding behavioral modification to medication therapy. For other domains of functions (oppositional behaviors, peer relationships, social skills, and reading achievement), the combination of behavioral and medication management was slightly superior to medication management or behavior management alone.[83,84] In addition, when looking at overall or global improvement across multiple domains and sites, combined treatment showed modest significant advantages over medication management (ES = 0.26).[46] Another advantage of combination treatment was the need for lower doses of stimulant medication compared with the medication group. For those children with comorbid anxiety disorders, and for low socioeconomic families, behavioral treatment was significantly better than community care and had similar efficacy to combined and medication management.[83,84] A follow-up of these children at 24 months, 10 months after the end of the study, revealed a persistence of superiority of the combined and medication management group over the behavioral modification and community groups, albeit at a reduced ES (50% of ES at the end of 14 months).[85,86] Of some concern, those children most consistently on medications showed significantly reduced height gain compared with those children not on medication.

In summary, the results of the MTA study indicated the long-term efficacy and effectiveness of psychostimulant medication for the core symptoms of ADHD, and added benefit of intensive behavioral therapy at home and in school for improving non-AHDH domains of functioning. Behavior modification by itself was not shown to be better than community care. However, the results of the MTA study should not be construed as proving that behavioral management is ineffective. Results related to the lack of efficacy of unitary behavioral management must be viewed within the context of the limitations of the MTA study. Most children in the community sample were taking medication, so behavioral management was being compared to another treatment (community medication management), not to no treatment or placebo. When children with behavioral management were compared to the unmedicated children in the community, they had superior reduction in ADHD symptoms.[84]

Unfortunately, although the MTA was longer term than most other studies, it did not address true long-term effectiveness. The important questions concerning effectiveness in improving education and social outcomes by adulthood, without significant long-term side effects, remain to be answered. In addition, both types of treatment, medication management and behavioral modification, were far more intensive than services generally available to most families. For example, the behavioral management component included 27 group and 8 individual parent-training sessions, an 8-week therapeutic summer camp experience for each child, 10 to 16 biweekly sessions of teacher consultations concerning behavior management, and 12 weeks of a behaviorally trained aide working directly with the child.[83] How results from such an intensive behavior medication regimen compare to results of behavior therapy likely to be available to families in most communities is unknown.

Concerns About Use of Psychostimulant Medication in Preschool Children

A population-based analysis of state Medicaid program data by Zito and colleagues revealed that 1.2% of 2- to 4-year-olds were receiving stimulant medications in 1995. More than 2% of 4-year-olds were receiving methylphenidate and prescriptions of stimulant medications to preschoolers increased 2- to 3-fold in the from 1991 to 1995.[87] In another study of state Medicaid data, over half of children 3 years of age or less with the diagnosis of ADHD were receiving stimulant medications, and one-third of these young children were receiving two or more psychotropic medications.[88] Concerns about this extensive use of psychostimulants in very young children were raised in the academic community[89-91] and by the public.

Effect on Neurodevelopment. Most of these concerns were focused on dangers to a changing and very plastic nervous system and the potential for altering the course of neurodevelopment. Studies on rats have not been reassuring. In a study in prepubertal rats by Moll and colleagues, density of dopamine transporters in the striatum was significantly reduced after early methylphenidate administration.[92] The decline was long-lasting and reached 50% by adulthood. Several other studies in rats given methylphenidate also show changes in the function of brain dopamine cells. These studies also indicate that exposure to methylphenidate causes changes in behavior including alteration of responses to cocaine when the rat reaches adulthood, depressive-like symptoms, and anxiety.[93-95] Thus early exposure to psychostimulants may have delayed effects on anatomy and behavior that are not obvious until adolescence or adulthood. These effects appear to be more extensive and permanent than when exposure occurs at older ages.[96] While one cannot extrapolate from rats to humans directly, and while animal studies raise concerns about the use of psychostimulants *throughout* childhood, these studies raise most serious concerns about use in very young children.

Effect on Linear Growth. The relationship of ADHD to linear growth is complex. The disorder itself could be associated with altered central nervous system growth factors, or with increased caloric expenditures. Psychostimulant drugs may have direct central nervous system effects on growth factors or could decrease linear growth through decreased appetite and caloric intake. It has been long recognized that children with ADHD on psychostimulants have slowed growth over 1 to 2 years.[97,98] Several studies have indicated that when medication is stopped, either temporarily on "drug holidays," or permanently, there is growth rebound.[99] Klein and colleagues ultimately found no significant decrease in final height in a cohort of ADHD children followed through adolescence and into young adulthood.[100,101] Spencer and colleagues studied children and adolescents with ADHD and found an approximately 2-cm height deficit in those with ADHD.[102] They also found that 10% of the ADHD group were more than 2 standard deviations below the average height for age. The height deficits were only evident in early adolescence and seemed unrelated to psychostimulant treatment or weight loss. The authors postulated that the deficits were due to catecholamine dysregulation in children with ADHD, and not due to psychostimulants. The MTA study found growth suppression directly related to use of psychostimulants, implying that lower growth rates seen in children with ADHD are due to medication use and not to their disorder.[86]

In summary, children with ADHD seem to have modest deficits in linear growth. While these deficits may be related to the disorder itself, there is evidence that psychostimulant use causes at least temporary deficits in linear growth. There are no studies looking at linear growth in young children on psychostimulants. However, the more rapid growth rate of the young child raises concerns about growth suppression at such a young age.

Efficacy and Safety of Psychostimulants in the Treatment of Preschool Children with ADHD

There have been 10 double-blind placebo controlled trials looking at efficacy of methylphenidate in the treatment of preschool children with ADHD (Table 4).[103-112] Very few children below 4 years of age were included in the studies, and almost none were less than 3 years of age. There are no controlled trials of amphetamines, long-acting stimulants, or pemoline in the preschool age group, nor are there any published data on the efficacy or safety of atomoxetine, a nonstimulant selective norepinephrine reuptake inhibitor approved by the FDA for treatment of ADHD in children 6 years of age and older. As compared to trials of psychostimulants in older children, adolescents, and adults, which numbered 150 in 1996,[81] this small number of studies on preschool children gives us limited information concerning efficacy and safety of these drugs. The total number of children with ADHD in all 10 studies of preschool children was 246, compared to over 5000 school-aged children, adolescents, and adults in studies in those age groups.[81]

Efficacy. Table 4 summarizes the results of these studies. All but one[106] of the studies found that methylphenidate was statistically superior to placebo, although outcome measures were varied. Only three of the studies used DSM-IV criteria to diagnose ADHD, and only one used DSM-IV symptomatology as an outcome measure. A number of the studies had very small numbers of subjects. Trials were of short duration, with most studies lasting only several weeks. Therefore these studies do not elucidate the long-term effectiveness or safety of psychostimulants in preschool children, even if the MTA definition of "long-term," 14 months, is used. When effect sizes of

TABLE 4. Double-blind placebo-controlled trials of methylphenidate in preschool children with ADHD symptoms

Study	No. preschool subjects	Age (months)	Diagnostic criteria	Duration and study design	MPH[a] dose	Results: efficacy and side effects
Conners, 1975[107]	59	<72; Mean = 58	Hyperactive and impulsive symptoms (maternal complaint)	42 days on drug or placebo (randomized controlled trial)	Average dose 12 mg/day; 0.75 mg/kg bid	Efficacy: improvement in hyperactive-impulsive symptoms based on physician and mother assessment; improvement on intelligence and visual-motor tests Side effects: minimal
Schleifer et al, 1975[111]	26	40–58; Mean = 49	Hyperactive and aggressive by psychiatric interview of mother	42 days (21 days on meds, 21 days off in randomized crossover design)	Average dose 5 mg bid, range 2.5 to 30 mg per day	Efficacy: improvement in hyperactive symptoms (ES[b] ~1.0); no improvement in nursery school observations or psychological lab testing Side effects: Most children experience significant side effects (sadness, irritability, social withdrawal, insomnia, anorexia). Only three mothers chose to continue meds.
Cohen et al, 1981[106]	24	Kindergarten age	Parent and teacher Conners' scale	3 months of cognitive-behavioral therapy, MPH[a], both, none by randomized assignment	10–30 mg/day	Efficacy: no differences among groups in behavior ratings or psychological testing, but too few subjects to have adequate power. Side effects: not measured
Barkley et al, 1984[104]	18[c]	48–71; Mean = 61	Parent/teacher complaint and Conners' Parent Scale	21–30 days (7–10 days each on placebo, low dose, higher dose MPH[a] in randomized crossover design)	0.15 mg/kg bid or 0.50 mg/kg bid	Efficacy: increase in compliance and decrease in off-task behaviors in structured play; no difference in response between preschool and school-aged children. Side effects: higher dose produced more side effects that lower dose or placebo; no difference in side effects between preschool and school-aged
Barkley, 1988[103]	27	31–59; Mean = 47	Physician diagnosis, parent complaint, and Conners' Parent Scale	21–30 days (7–10 days each on placebo, low dose, higher dose MPH[a] in randomized crossover design)	0.15 mg/kg bid or 0.50 mg/kg bid	Efficacy: increase in compliance (ES[b] ~0.6) and decrease in off-task behaviors (ES[b] ~0.5) during structured play at higher dose only Side effects: no statistical differences in treatment groups compared to placebo in number or severity of side effects
Mayes et al, 1994[109]	14[c] (10/14 had developmental disabilities)	22–60	DSM-III-R criteria based on physician assessment	On average 26 days (9 off meds, 8 on meds, 9 off meds)	Starting dose 0.3 mg/kg tid, increased based on response	Efficacy: improved parent rating scales of ADHD symptoms (71%) Side effects: 50% had some side effects (most common—irritability, anorexia, lethargy); no difference in rates between preschool and school-aged children
Mustin et al, 1997[110]	31	48–70	DSM-III-R criteria based on parent rating scale	21–30 days (7–10 on each dose, including placebo in randomized crossover design)	0.3 mg/kg bid or 0.5 mg/kg bid	Efficacy: improved parent rating scales of ADHD symptoms (ES[b] low dose ~0.5–0.7; ES[b] high dose ~0.8–1.0); improved cognitive measures of attention Side effects: Mild side effects, only seen at higher dose

TABLE 4. Double-blind placebo-controlled trials of methylphenidate in preschool children with ADHD symptoms (continued)

Study	No. preschool subjects	Age (months)	Diagnostic criteria	Duration and study design	MPH[a] dose	Results: efficacy and side effects
Byrne et al, 1998[105]	16; 8 ADHD 8 controls	48–72; Mean = 63	DSM-IV by 2 psychologists; Conners' Parent Rating Scale	5 months; case-control, before-after treatment design	5–10 mg bid or tid as prescribed by community physician[d]	Efficacy: improved parent rating scales of AHDH symptoms, attention, and social skills; improvement in laboratory measures of continuous performance and attention Side effects: not measured
Handen et al, 1999[108]	11 (all with developmental disabilities)	48–61; Mean = 59	Teacher rating on behavior questionnaire and Conners' Parent Rating Scale	21 days (7 days on each dose, including placebo in randomized crossover design)	0.3 mg/kg or 0.6 mg/kg q am, or bid or tid	Efficacy: improved teacher rating scales of ADHD symptoms (ES[b] ~1.3–2.0) at higher dose; 73% judged to be "responders" (40% decrease in Conner's score) Side effects: 45% had side effects, especially dullness, social withdrawal, anorexia; side effects more severe at higher dose
Short et al, 2004[112]	28[e]	48–71; Mean = 63	DSM-IV criteria based on parent rating scale	21–28 days (7 days on each dose, including placebo in randomized crossover design)	5 mg, 10 mg, and placebo bid; some of older children also given 15 mg bid	Efficacy: improved parent rating scales of DSM-IV ADHD symptoms on best dose (5 or 10 mg for most); 68% on treatment "normalized" (T score <60) versus 22% on placebo; similar improvement on teacher ratings Side effects: 15% experienced mild side effects, none causing termination of treatment

[a]Methylphenidate.
[b]Effect size: differences between groups expressed in units of standard deviations.
[c]Study included both preschool and school-aged children; number of subjects and age of subjects represents number and age of preschool children.
[d]Two of eight children with ADHD on d-amphetamine; six of eight children with ADHD on methylphenidate.
[e]Twenty-two children on methylphenidate bid, six children on mixed amphetamine salts q am.

improvement were measured or could be determined, they ranged from 0.50 to 1.00 in typically developing children. Most studies indicated that higher doses (0.5 to 0.6 mg/kg/dose) were more likely to show efficacy than lower doses (0.15 to 0.30 mg/kg/dose). In general, children received doses of methylphenidate of 5 to 10 mg twice daily. None of the studies, however, addressed determining appropriate starting doses for this age group or evaluated titration to most effective dose. When school-aged children were included in the studies, no difference in response to medication was seen between school-aged and preschool-aged children.

Safety. Eight of the studies reported on side effects as well as efficacy (Table 4). Most reported that side effects were mild.[103,104,107,110,112] In contrast, Shleifer and colleagues found that most children experienced significant side effects, which led to discontinuance of medication.[111] Two studies included school-aged children as well as preschool children and reported no differences in frequency of side effects based on the age of the child.[104,109] Two of the studies focused on developmentally disabled children and found an increase in side effects in this group of children, with side effects seen in approximately 45 to 50% of children given methylphenidate.[108,109] In general, higher doses of medication produced more side effects.[104,110]

Firestone and colleagues re-examined the data from their efficacy study and reported in detail on side effects seen in preschool children.[113] Significant side effects were only reported in higher doses of methylphenidate (0.5 mg/kg/dose) as compared to placebo. Lower doses (0.3 mg/kg/dose) showed no increase in side effects. Sadness, anorexia, drowsiness, social withdrawal, and nightmares were the side effects that occurred more frequently at higher dose methylphenidate. For example, anorexia was seen in 81% of children on higher dose methylphenidate, and social withdrawal was seen in 75% of children on the higher dose. These side effects were severe in 19% (sadness), 22% (anorexia), 16% (drowsiness), 12% (social withdrawal), and 6% (nightmares) of these children. While most children experienced mild side effects, the frequency and severity of these side effects appear to be greater than that reported in school-aged children.[114] Of additional concern, decreased caloric intake and

social withdrawal could have more long-term negative effects on young children going through rapid physical and mental growth. Unfortunately, while lower doses of methylphenidate seemed to cause few side effects, lower doses were also much less likely to be efficacious in improving ADHD symptomatology.

Certain symptoms, often considered to be side effects of methylphenidate, actually decreased with treatment in some studies.[112,113] Irritability, insomnia, and anxiety significantly decreased in frequency and severity in children taking higher doses of methylphenidate. Thus, these symptoms are most likely due to ADHD itself and are therefore ameliorated by treatment with methylphenidate.

Preschool ADHD Treatment Study (PATS). To address the gaps in our knowledge in the efficacy and safety of stimulant medication in young children, the National Institute of Mental Health funded the Preschool ADHD Treatment Study (PATS), a multisite, randomized controlled trial of methylphenidate in children 3 to 5.5 years of age.[115] The PATS has the following phases:

1. Parent Training: Families participate in 10-week parent training. Those children not demonstrating a decrease in ADHD symptoms of 30% or greater are asked to enter the methylphenidate trials.
2. Titration Trial: As in the MTA study, subjects are entered into a 5-week double-blind, randomized within-subject crossover design trial to determine optimal dose of methylphenidate. Starting dose in the PATS is 1.25 mg tid and the maximum dose is 10 mg tid.
3. Parallel Trial: Subjects are then entered into a 4-week double-blind, randomized, placebo-controlled study at their optimal dose. Clinical response was defined as at least a 25% decrease of ADHD symptoms based on parent–teacher ratings.
4. Open-Label Trial: 42 weeks of open-label treatment to assess safety.
5. Discontinuation Trial: At the end of the open-label trial, subjects are randomized to either methylphenidate or placebo for a 6-week period.

Results of the PATS have not yet been published, but have been presented at several scientific meetings. At the American Academy of Child and Adolescent Psychiatry Annual Meeting in October 2004, the PATS investigators shared preliminary results.[116] Most children did not sufficiently respond to the parent-training program. Eighty-five percent of preschool children responded to methylphenidate in the titration trial. This response rate is comparable to the 77% response rate of school-age children in the MTA study.[117] Most children were titrated to an optimal dose of methylphenidate between 1.25 and 7.5 mg tid. A small number of children required 10 mg tid. Effect sizes of response in preschool children, however, were somewhat smaller than those found for school-age children in the MTA study.[117] In the parallel trial, slightly less than half of the children on methylphenidate had clinically significant decreases in ADHD symptomatology. Side-effect data and longer term (42 week) efficacy data have not yet been reported.

Summary of Efficacy and Safety Data. Methylphenidate appears to be efficacious in the treatment of ADHD symptoms and impairment in preschool children. Effect sizes of the decrease in ADHD symptomatology are somewhat smaller in preschool children than in school-aged children. Doses of approximately 5 mg tid are generally effective. A broad range of doses may be optimal for the individual child, however, ranging from 1.25 to 10 mg/dose. Side effects are usually mild, but the frequency and severity of side effects are greater than in school-aged children. Side effects such as social withdrawal and anorexia are even more a matter for concern in the rapidly developing preschooler than in the school-aged child. Almost no children under the age of 3 years have been studied, and therefore, medication has unknown effects and safety in those children. Results from the PATS, as they become available, will further our understanding of the efficacy and safety of methylphenidate in young children.

Other Concerns Regarding the Use of Psychostimulants in Preschool Children. Several other issues face the practitioner who considers using stimulants in the treatment of preschool children with ADHD. Oddly, while all the randomized controlled trials studying the efficacy of stimulants in preschool children, including the PATS, have studied methylphenidate, the Food and Drug Administration approves product labeling for amphetamine preparations for ADHD down to age 3 years and for methylphenidate down to age 6 years.[27] Thus the clinician is forced to use methylphenidate in preschool children as an off-label drug, while at the same time is able to use amphetamines in preschool children with much less knowledge of efficacy and safety. There is also no known starting dose for preschool children. The PATS used 1.25 mg tid as the starting dose, and some of the

children were found to have this dose as their "best dose."[32,116] Therefore, at this time, 1.25 mg would seem a reasonable starting dose. However, since the lowest strength tablets available are 5 mg, the clinician is forced to ask parents to cut tablets in quarters. Furthermore, swallowing pills is problematic for preschoolers. Either these young children have to be taught to swallow pills using behavioral training, or their parents need to find a pharmacy that will prepare a liquid suspension, or their parents have to crush the pill in applesauce themselves. All of these issues may lead to inaccurate dosing or nonstandard absorption dynamics.

Efficacy of Behavioral Treatments for ADHD in Preschool Children

Behavioral Treatments for School-Age Children. A number of psychosocial treatments have been shown, at least in the short term, to be useful in the treatment of ADHD in school-aged children. Clinical behavior therapy involving either parent training, teacher training, direct contingency management by trained behavioral staff in a school setting, or intensive packaged behavioral treatments (combinations of parent and teacher training, often combined with direct contingency management) are empirically supported by the research literature for school-aged children with ADHD.[82] In contrast, cognitive-behavioral interventions have not been shown to produce important changes in the behavior or academic achievement of school-aged children with ADHD.[82] While the intensive packaged behavioral treatment of the MTA study[118,119] was not found to be better than the routine treatment community comparison,[83] as was pointed out previously in this article, there are several cautions about the over-interpretation of this data. First, the majority of the children (two-thirds) in the routine community comparison were receiving stimulant therapy.[84] Therefore, the behavioral treatment was being compared to a suboptimal stimulant treatment comparison group rather than a placebo or wait-list control group. Furthermore, secondary analyses indicated that the behavioral treatment was superior to routine community treatment in certain subgroups (children with anxiety and low socioeconomic groups),[84] and combining behavior therapy with medication allowed for a lower medication dose.[83,85] The clinical practice guideline of the American Academy of Pediatrics states that clinicians should recommend stimulant medication and/or behavior therapy as appropriate treatment for children with ADHD.[120] However, the strength of the evidence is only fair for behavior therapy, whereas it is strong for stimulant medication. The practice parameters issued by the American Academy of Child and Adolescent Psychiatry recommends medication, along with support and education of parents and appropriate school placement, as "the cornerstones of treatment" and lists behavior modification among "other treatments" to address "remaining symptoms."[121]

Reasons for Serious Consideration of Behavior Therapy in Preschool ADHD Children. There are several reasons to consider behavior therapy as a treatment option even more seriously in preschool children than in school-aged children. There is a reluctance on the part of most parents to start young children on psychostimulant medication.[122] There is also concern among developmental-behavioral pediatricians and child psychiatrists about the long-term side effects of psychostimulants on the young brain and body.[27,32,89-91,123] Therefore, the American Academy of Child and Adolescent Psychiatry recommends that clinicians consider starting stimulant medication only in the most severely symptomatic children and only after a failed trial of behavioral therapy.[121] Reflecting these recommendations, the PATS had a built-in trial of behavior therapy preceding its medication trials.[115,123,124]

In addition to these concerns about the safety and acceptability of psychostimulant medication in preschool children, there are theoretical reasons to believe that behavior therapy may be more effective in younger children. In school-age children, ADHD symptoms have often become complicated by school failure and rejection by peers. These problems may lead to low self-esteem and a sense of demoralization in the child with ADHD, which makes the child more difficult to treat with behavioral modalities.[125,126] Psychosocial interventions in the preschool period may be more effective because the intervention is occurring prior to the establishment of these additional psychological problems.

Parent-Training Programs for Preschool Children with ADHD. Preschool children with ADHD may be considered to have two different categories of behavior that may be amenable to behavior therapy: (1) noncompliant behavior due either to their ADHD and/or to associated ODD, and (2) ADHD core symptoms of hyperactivity, distractibility, and impulsivity. Parent-training programs have generally focused on

the noncompliant behavior rather than core ADHD symptoms. The elements of most parent-training programs have included instructing parents in the (1) use of positive reinforcement of pro-social behavior; (2) withdrawal of attention for misbehavior through the use of ignoring or time-out rather than negative reinforcement of misbehavior through aversive techniques; (3) the appropriate issuing of commands and reprimands.[122,127] Parent training is done in either group or individual sessions. Parent-training programs using these types of techniques have been shown to be effective in reducing noncompliant behavior in children with ODD, ADHD, and ODD + ADHD, as well as improving parenting skills in the parents of these children.[128-131] However, in those studies that measured core ADHD symptoms as an outcome, no significant effect was seen on the core ADHD symptoms.[129,131]

Sonuga-Barke and colleagues have studied the expansion of parent training beyond standard behavioral management techniques. In addition to standard behavioral management, the parent-training program they designed promoted (1) effective limit setting; (2) clarity in communications and establishment of routines as a basis for authoritative parenting; and (3) a tailored promotion of improved attention and self-regulation of the child. The treatment was given during eight 1-hour weekly visits with one of two specially trained health visitor therapists in each family's home. A randomized controlled trial of this program was performed with comparison subjects assigned to supportive parent counseling or wait-list controls.[122,132] Children were identified at 3 years of age. Results of this study were encouraging, with parent training producing substantial statistically significant improvement in core ADHD symptoms as well as ODD symptoms when compared to either parent counseling or wait-list conditions. The effects persisted 15 weeks after the end of the 8-week treatment program. Effect sizes for improvement of ADHD symptoms were 0.69 and 0.87 for observed and parent-reported symptoms, respectively. However only 53% of patients met criteria for a clinical response to parent training, implying that almost half of preschool children with ADHD will still need to be considered for other therapies (including stimulant medication). Furthermore, when the investigators repeated their intervention with a group of nonspecialist nurses in a primary care setting, there was no reduction of ADHD symptoms.[133] This would imply that generalizing the results of the original study to multiple and diverse sites will be difficult. The difficulty of maintaining the integrity of intervention techniques, and therefore the efficacy of the intervention, when transferring a highly specialized intervention to a less structured environment was also encountered by Barkley and colleagues. They attempted to institute an evidence-based behavior therapy parenting program in a school system at kindergarten entry. Parents of children identified with ADHD and ODD symptomatology were offered 10-week parent-training program, but very poor attendance led to no significant change in ADHD symptoms or disruptive behavior.[134]

A secondary analysis of the results of both of the Sonuga–Barke studies described above was performed by the investigators. This analysis revealed that the presence or absence of maternal ADHD was an important factor in the child's response to the parent-training program. Those children whose mothers had high ADHD symptomatology had no response to the intervention, while those children whose mothers had low ADHD symptomatology responded quite well. The association of maternal ADHD symptoms with their child's response to the parent-training program persisted after controlling for the intensity of the child's ADHD symptoms, the family's SES, maternal mental health, and other factors in regression analyses.[135] The authors discuss possible mechanisms for the importance of maternal ADHD, including cognitive and organizational impairment of the mother, maternal difficulties in interpersonal relationships, and maternal motivational style. They also suggest the possibility that ADHD diagnosed in children with parents exhibiting a high level of ADHD symptoms may be more biogenetically based and may therefore be more likely to require psychopharmacologic therapy.

Behavioral Interventions in the Preschool Setting. There is little known about ADHD interventions in the preschool setting, through either teacher training or direct contingency management of the child. Barkley and colleagues studied 5-year-olds in kindergarten and provided an intensive behavioral program that included teacher and teacher aide training; an intensive token system; response cost, over-correction, and time-out from reinforcement; group social skills training, cognitive-behavioral self-control training, and anger training; a daily school report card of behavior with home-based reinforcement; targeted behavior modification at recess and bus rides; and academic

skills training. Results indicated a reduction of hyperactive, impulsive, inattentive, and aggressive behavior as well as improvement of social skills and self-control in disruptive children.[134] However, evaluators were not blinded to the treatment status of the children and that may have biased their assessments to more positive outcomes. In addition, the behavioral improvements in the school kindergarten did not generalize to the home environment, and there was no evidence of improvement of academic achievement. Finally, these children were "older" preschool children, and generalization of these findings to 3- and 4-year-olds in preschool settings is not possible. One other study, by McGoey and colleagues, examined the effects of a teacher training program using positive reinforcement and cost-response intervention on the disruptive behavior of preschool children with ADHD. Direct observations of behavior indicated decreases in disruptive behavior, but no measurement of core ADHD symptoms was included.[136]

Summary of Behavioral Interventions for Preschool Children with ADHD. There is reasonable evidence that parent-training programs improve noncompliant and disruptive behavior in preschool children with ADHD. There is only one study, however, that has looked for, and found, a clinically significant effect of parent training on core ADHD symptoms. Behavioral interventions in the preschool setting, involving teacher training or direct contingency management of children, are more poorly studied than parent-training interventions. No firm conclusions about their effectiveness can be reached. Multimodal treatment studies of preschool ADHD, looking at combined medication and behavioral therapies, do not exist.

The effectiveness of parent-training programs appears to be dependent on maintenance of the integrity of the intervention with highly specialized and committed professional staff. Availability of large numbers of such professionals in most communities is problematic. Yet, without such professionals, programs do not appear to be effective. Parent-training programs also seem to be ineffective when parents themselves, as commonly occurs, have ADHD. Furthermore, approximately 50% of children will show a clinical improvement when their parents are enrolled in such programs, leaving the other half of children with ADHD in need of alternative treatments. Finally, while many parents reject pharmacological treatment of their preschool children with ADHD, parents find the large commitment they need to make to behavioral treatments difficult to sustain. As a result, parents are frequently nonadherent to required attendance at training sessions, especially if the sessions are offered at clinical facilities and not in local community or home settings.[137] Thus the clinician is frequently left with the conundrum of wanting to avoid stimulant therapy for preschool children with ADHD, but being unable to provide alternative evidenced-based, acceptable behavioral therapy programs to families.

Summary and Conclusions

Diagnosis and Prevalence

- Despite concerns about the applicability and wording of DSM-IV criteria for the diagnosis of ADHD in preschool children, DSM-IV-based ADHD parent and teacher rating scales, developed for use with school-age children, have been shown to be reliable when used with preschool children.
- The overall prevalence rate of ADHD in preschool children is 4.9% This prevalence rate is similar to the prevalence rate of ADHD for school-aged children (5.8%).
- The prevalence rates of ADHD subtypes in preschool children are markedly different from that in school-aged children. Most school-aged children have either the inattentive (48%) or the combined (43%) subtypes and very few have the hyperactive-impulsive (9%) subtype. In comparison, for preschool children prevalence rates of the inattentive and hyperactive-impulsive subtypes are reversed. Forty-eight percent of preschool children are diagnosed with the hyperactive-impulsive subtype and only 13% are diagnosed as having the inattentive subtype.
- Gender differences are less pronounced in preschool children than in older children. The ratio of boys to girls diagnosed with ADHD in the preschool age group is 2:1, compared to 3:1 in school-aged children.
- Preschool children are likely to have comorbidities, especially ODD. At least half of preschool children with ADHD have a comorbidity (ODD, CD, depression, anxiety) and in approximately one-third of the cases there are two or more comorbidities. The addition of the diagnosis of ODD is likely to be a marker for more severe ADHD symptomatology. Even those children without the diagnosis of ODD are likely to have some oppositional behaviors.

- Despite concerns about the overdiagnosis of ADHD in preschool children, the DSM-IV criteria appear to be valid for diagnosis of ADHD in this age group. There is ample evidence that young children identified by DSM-IV criteria as having ADHD have significant impairments in psychosocial and academic functioning, including impaired relationships with parents, siblings, teachers, and peers; school suspension; deficient social skills and preacademic skills; and increased incidence of accidental injury. There is also stability of ADHD symptoms and diagnosis, as well as psychosocial and academic impairment, from the preschool period into school age. The construct validity of DSM-IV criteria in preschool children is supported by finding a "dose effect" of number of symptoms on impairment, and a neuropsychological profile similar to that in school-aged children.

Treatment

- The treatment modalities that are available for preschool children are the same as for school-aged children: psychostimulant medication and behavior therapy.
- Families, clinicians, researchers, and the public have strongly felt concerns about the use of psychostimulants in young children. These concerns are based on potential dangers to a changing and plastic nervous system, including altering the course of neurodevelopment. There is scientific evidence from animal experiments to support these concerns.
- There is controversy over whether psychostimulant medication causes permanent deficits in linear growth in school-aged children and adolescents with ADHD. However, school-aged children with ADHD on psychostimulants appear to have modest deficits in linear growth, at least in the short term. There are no studies looking at linear growth in young children on psychostimulant medications. However, the more rapid growth rate of the young child raises concerns about growth suppression at such a young age.
- Based on a small number of double-blind placebo controlled studies, and preliminary information from a new multicenter randomized controlled trial (PATS), methylphenidate appears to be efficacious in the treatment of ADHD symptoms and impairment in preschool children. Effect sizes of the decrease in ADHD symptoms are somewhat smaller in preschool children than in school-aged children. Methylphenidate doses of 5 mg tid are generally effective, although a broad range of doses (ranging from 1.25 to 10 mg/dose) may be optimal for the individual child. It seems prudent to start with a dose of 1.25 mg, especially in the 3- to 4-year-old.
- Side effects are usually mild, but the frequency and severity of side effects are greater than in school-aged children. Side effects such as social withdrawal and anorexia are even more a matter for concern in the rapidly developing preschool child than in the school-aged child.
- Because of concerns about safety, the American Academy of Child and Adolescent Psychiatry recommends that clinicians consider starting psychostimulant medication only in the most severely symptomatic preschool children and only after a failed trial of behavioral therapy.
- There is no information on the efficacy and side effects of psychostimulants under the age of 3. The clinician should be wary of prescribing psychostimulants to children under the age of 3 for the diagnosis of ADHD.
- Results of the PATS, as they become available, will further our understanding of the efficacy and safety of methylphenidate in young children.
- There is evidence that behavioral-based parent-training programs improve noncompliant and disruptive behavior in preschool children with ADHD. However, there is only preliminary research on the design and effect of parent-training programs on core ADHD symptoms. While this research shows promising results, efficacy depends on the availability of appropriately trained and supervised professionals in the local community. Parent training also seems to be ineffective when the parent has ADHD. Many parents find the large commitment of time and effort required by parent-training programs difficult to sustain. Therefore, while behavioral therapy programs are recommended as the first line of treatment for preschool ADHD, effective and accessible programs may not be available to families in many communities.

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