Evidence Base for the Use of Stimulant Medication in Preschool Children With ADHD

Scott H. Kollins, PhD; Laurence Greenhill, MD

Increasingly, attention-deficit/hyperactivity disorder (ADHD) is being recognized as a valid disorder in preschool-aged children. There are only limited data available, however, to provide useful guidelines for the pharmacological management of this impairing condition in this age range. This article (1) reviews the available studies on stimulant treatment in preschoolers with ADHD; (2) provides an overview of the recently completed National Institute of Mental Health-funded Preschool ADHD Treatment Study (PATS); (3) highlights special considerations in conducting psychopharmacological research in this age range; and (4) provides clinical guidelines for managing the ADHD in preschoolers on the basis of available evidence. Key words: attention-deficit/hyperactivity disorder, methylphenidate, preschoolers, stimulant medication

The prevalence of attention-deficit/hyperactivity disorder (ADHD) in preschool-aged children is estimated to be approximately 2% (Lavigne et al., 1996), although other studies have suggested rates as high as 6% and 18%, respectively, based on parent and teacher ratings of a community sample of children aged 3 to 5 years (Gadow, Sprafkin, & Nolan, 2001). Regardless of actual prevalence, ADHD symptoms cause significant impairment across home, school, and social domains of functioning in the preschool-age group and increase risk for significant levels of both internalizing and externalizing comorbid psychopathology (DuPaul, McGoey, Eckert, & VanBrakle, 2001; Keenan & Wakschlag, 2000; Lahey et al., 1998; Wens et al., 2002).

There are a number of important considerations when assessing the ADHD in this age range and many of these will be discussed in a separate paper (see Eggers, this issue). The purpose of this report, therefore, was (1) to summarize the literature on pharmacological treatment of preschoolers with ADHD with stimulant medications, including what is currently known about efficacy, safety, and prescribing trends; (2) to provide an overview of the recently completed Preschool ADHD Treatment Study (PATS) and in doing so to highlight some of the controversial issues involved in conducting clinical trials in this age range; and (3) to provide recommendations for clinicians seeing preschool children with ADHD.

STIMULANT TREATMENT IN PRESCHOOL CHILDREN WITH ADHD

Efficacy

Studies of short-term efficacy of stimulant medication constitute one of the largest bodies of treatment literature for any childhood psychiatric disorder and suggest that the vast majority of school-age children treated with stimulant drugs show improvement in core ADHD symptoms (Greenhill et al., 2002). In contrast to the hundreds of well-controlled trials that have been conducted with school-age...
children, only a handful of studies have been published that explicitly assess stimulant drug effects in preschool-aged children with ADHD (Greenhill, 1998). Table 1 illustrates the 10 published studies that have been conducted to date.*

Of these studies, all evaluated methylphenidate, which is ironic given that Food & Drug Administration (FDA) guidelines for methylphenidate-based products do not recommend use in children younger than 6 years. One of the studies evaluated the efficacy of both methylphenidate and mixed amphetamine salts (Short, Manos, FIndling, & Schubel, 2004). These studies do provide some evidence for the efficacy of methylphenidate in preschool-age children, as most of these studies (7/9; 78%) reported that methylphenidate improved ADHD symptomatology in at least one setting. The most recent of these studies found that the best dose of stimulant drug (in a crossover design) significantly improved parent and teacher ratings and reduced parent ratings from a significant level (t score >70 on placebo) to within the reference range (t score = 52.5 on best dose; Short et al., 2004).

In spite of the evidence supporting the efficacy of stimulants in preschool children with ADHD, there are limitations to many of these studies that preclude drawing strong conclusions. First, the sample sizes for these studies found that the best dose of stimulant drug (in a crossover design) significantly improved parent and teacher ratings and reduced parent ratings from a significant level (t score >70 on placebo) to within the reference range (t score = 52.5 on best dose; Short et al., 2004).

As shown in Table 1, these studies have not all used consistent approaches for diagnosing the ADHD among the preschool children. Given some of the unique challenges to establishing a diagnosis in children this young (see Egger, this issue; Greenhill et al., 2003), variance in the diagnostic methods makes it very difficult to ascertain whether comparable clinical groups were being compared across studies. The studies in question have also been short in duration with limited prospective follow-up, have had low and/or restricted dose ranges, and have not used data collected from informants other than parents. This methodological variance precludes pooling of data and makes it difficult to glean a consistent picture of the safety and efficacy of methylphenidate in this age range (Greenhill, 1998).

Safety

The data from preschool studies of stimulant treatment are somewhat more mixed with respect to safety. While there is little evidence that substantial numbers of patients withdrew from the trials due to adverse effects of the medications, there are some data suggesting that the proportion of children experiencing side effects may be higher than that observed in school-aged children, and that the nature of the side effects might be different than that observed in older patients. For example, Handen et al. (1999) reported that 45% of their sample of 11 children reported adverse events (AEs). These data are somewhat difficult to interpret, however, because the patients in this study also met criteria for developmental disabilities. This study and others (eg, Firestone et al., 1998; Short et al., 2004) reported that some of the most commonly reported side effects were irritability, crying, and increased emotional outbursts. The frequency of these AEs seemed to be higher among preschoolers with ADHD compared with school-aged children.

Prescribing trends for preschoolers with ADHD

One potential barrier to research on stimulants in preschoolers is the FDA guidelines for age-appropriate stimulant use. While the FDA-approved package insert instructions indicate

*Note that these 10 published works represent 9 actual studies. Musten, Firestone, Pisterman, Bennett, and Mercer (1997) and Firestone, Musten, Pisterman, Mercer, and Bennett (1998) report on the same sample, with the former reporting efficacy and the latter reporting safety.
Table 1. Preschool ADHD stimulant trials*

<table>
<thead>
<tr>
<th>Study</th>
<th>Diagnosis</th>
<th>N</th>
<th>Design</th>
<th>Dose</th>
<th>Duration</th>
<th>Efficacy</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Schleifer et al., 1975)</td>
<td>Pediatrician</td>
<td>26</td>
<td>Crossover</td>
<td>0.6-mg/kg MPH</td>
<td>3 wk</td>
<td>Drug better</td>
<td>Dysphoric withdrawn</td>
</tr>
<tr>
<td>(Connors, 1975)</td>
<td>Physician</td>
<td>59</td>
<td>Parallel</td>
<td>11.8-mg MPH</td>
<td>6 wk</td>
<td>Drug better</td>
<td>No side effects</td>
</tr>
<tr>
<td>(Cohen, 1981)</td>
<td>Psychiatrist</td>
<td>24</td>
<td>Parallel</td>
<td>30-mg MPH</td>
<td>8 wk</td>
<td>No drug effect</td>
<td>No side effects</td>
</tr>
<tr>
<td>(Barkley, Karlsson, Strzelecki, &amp; Murphy, 1984)</td>
<td>Referring MD</td>
<td>18</td>
<td>Crossover</td>
<td>0.15- 0.5-mg/kg MPH</td>
<td>3 wk</td>
<td>No drug effect</td>
<td>No side effects</td>
</tr>
<tr>
<td>(Barkley, 1988)</td>
<td>Referring MD</td>
<td>27</td>
<td>Crossover</td>
<td>0.15- 0.5-mg/kg MPH</td>
<td>3 wk</td>
<td>On 0.5 dose, compliance ↑ 79% MPH group↓ active</td>
<td>MPH &gt; placebo</td>
</tr>
<tr>
<td>(Mayes, Citkes, Bixler, Humphrey, &amp; Mattison, 1994)</td>
<td>Referring MD</td>
<td>14</td>
<td>ABA design</td>
<td>10-mg MPH</td>
<td>24 d</td>
<td></td>
<td>MPH &gt; placebo</td>
</tr>
<tr>
<td>(Musten et al., 1997)</td>
<td>Referring MD</td>
<td>31</td>
<td>Crossover</td>
<td>0.3- 0.5-mg/kg MPH</td>
<td>30 d</td>
<td>↑ attention, ↓ hyperactivity (Montier Study)</td>
<td>0.5 mg/kg, 10% side effects</td>
</tr>
<tr>
<td>(Firestone et al., 1998)</td>
<td>Referring MD</td>
<td>31</td>
<td>Crossover</td>
<td>0.3- 0.5-mg/kg MPH</td>
<td>30 d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Handen et al., 1999)</td>
<td>Consensus diagnosis</td>
<td>11</td>
<td>Crossover</td>
<td>0.3- 0.6-mg/kg MPH</td>
<td>4 wk</td>
<td>0.6 dose &gt; 0.3 dose</td>
<td>45% had side effects</td>
</tr>
<tr>
<td>(Short et al., 2004)</td>
<td>Psychologist + psychiatrist</td>
<td>28</td>
<td>Crossover</td>
<td>5-, 10-, 15-mg MPH BID; 5-, 10-, 15-mg MAS QD</td>
<td>3–4 wk</td>
<td>Best dose &gt; placebo</td>
<td></td>
</tr>
</tbody>
</table>

*ADHD indicates attention-deficit/hyperactivity disorder; MPH, methylphenidate hydrochloride; and ABA, applied behavior analysis.
approval for use of amphetamine down to age 3, methylphenidate-based products carry a warning against its use for age less than 6 years. This labeling anomaly and the comparative lack of safety and efficacy information on stimulant use in preschool children with ADHD have not deterred physicians in practice from prescribing methylphenidate. Zito et al. (2000) reported a 1.7- to 3.1-fold increase in methylphenidate use between 1991 and 1995 in children 2 to 4 years old in 2 state Medicaid and 1 Health Maintenance Organization (HMO) databases, while DeBar, Lynch, Powell, and Gale (2003), using another large HMO database, found only infrequent utilization of pharmacotherapy among preschoolers. A more recent report cited a 49% increase in utilization of ADHD medication between 2000 and 2003 in children younger than 5 years (Medco Health Solutions, 2004). A number of other sources over the past 10 years provide converging evidence for the widespread use of methylphenidate in children younger than 6 years (FDA, 1997; IMS America, 1995; Kaufman, Malone, & Asante, 1996; Rappley, Gardiner, Tetton, & Houang, 1995).

The rapidly increasing use of methylphenidate hydrochloride (MPH) to treat preschoolers with ADHD had become a major public health concern, leading to its placement on a list published by the White House in 2000 as one of the highest priority medications requiring further research on safety and efficacy for use in pediatric populations. Public health concern in recent years has contributed to several important developments in the area of preschool clinical psychopharmacology. First, in 1999 the PATS was designed to address the critical gap in knowledge regarding safety and efficacy of stimulants in preschool children with ADHD. Second, the American Academy of Child & Adolescent Psychiatry (AACAP) sponsored a workshop in 2000 to address special challenges and obstacles involved in conducting psychopharmacology trials in preschool children. Representatives from academia, industry, and government attended this meeting, which generated recommendations and strategies for subsequent research (Greenhill et al., 2003).

THE PATS TRIAL AND ISSUES IN THE CONDUCT OF PSYCHOPHARMACOLOGICAL TREATMENT IN PRESCHOOL CHILDREN

Overview

The PATS was a 6-site, clinical trial funded through a cooperative agreement by the National Institute of Mental Health (NIMH) and the following research centers: Columbia/New York State Psychiatric Institute (NYSPI), Duke University, Johns Hopkins University, New York University, the University of California - Los Angeles, and the University of California - Irvine, in addition to the NIMH staff. Details regarding the design of the trial and primary outcomes are published separately (Kollins et al., in press; Greenhill et al., in press). The Columbia/NYSPI provided overall coordination and statistical functions. Data management was provided by the Nathan Kline Institute. Patients between the ages of 36 and 66 months who had been diagnosed with the ADHD were included and participated in an 8-phase, 70-week trial. The initial screening phase was used to rigorously characterize the sample for inclusion. Following Screening, caregivers of all patients participated in a 10-week parent training program. Following this intervention, a baseline assessment was conducted to determine eligibility for entry into the medication phases of the study. Eligible patients were then placed in a safety lead-in phase to ensure the doses to be tested in subsequent phases could be tolerated. Patients then underwent a 5-week double-blind crossover titration trial to determine efficacy and safety of 4 active doses of methylphenidate (1.25 mg, 2.5 mg, 5.0 mg, and 7.5 mg) and placebo. The primary outcome measure for the PATS was a composite of parent and teacher ratings across each of the doses during this 5-week crossover titration phase. Following this phase, a best dose was determined for each patient, and the patients were subsequently...
randomized to receive either this optimized dose or a placebo in a double-blind 4-week parallel phase trial. At the completion of this phase, patients entered a 10-month open-label maintenance phase to assess long-term impact of treatment. Finally, a subset of patients was enrolled in a double-blind placebo-controlled discontinuation trial where they were assigned to receive the dose they were on at the end of maintenance phase or placebo.

Major ethical concerns exist about including very young children in clinical trial research. Such young children would not be expected to understand the risks of such research. To explore these concerns further, the PATS protocol underwent further ethical and safety review by the Ethics Workgroup of the NIMH National Advisory Mental Health Council, the FDA’s Neuropharmacological Division, and the NIMH Data and Safety Monitoring Board (DSMB) prior to funding. In addition, the study’s outline was presented for discussion at the Research Forum of the Annual Meeting of the AACAP in 2000, where further recommendations were collected (Greenhill et al., 2003). Below, the design of the PATS trial is described in detail and decisions that were faced as a result of these considerations are highlighted. A more comprehensive set of papers describing the initial findings of the PATS trial will soon be available.

**Phase 1: Screening and enrollment**

All patients underwent a comprehensive assessment battery that was designed to maximize ADHD diagnostic validity for all enrolled patients. To be eligible for the study, patients had to meet both dimensional symptom criteria (both parent and teacher rating scale scores >1.5 SD above age- and gender-adjusted mean for preschoolers) and categorical diagnostic criteria (positive diagnosis on *Diagnostic Interview Schedule for Children Version IV* and semi-structured diagnostic interview). Furthermore, all cases were presented to a cross-site panel of clinicians and only those patients for whom there was consensus agreement that all inclusion and no exclusion criteria were met could be enrolled into the study. The screening procedures and approach for establishing diagnostic validity were guided by recommendations from both the FDA and the Ethics Workgroup of the NIMH to include only the most severe cases and for whom impairment and multi-setting symptomatology could be established (eg, Greenhill et al., 2003). Moreover, patients were required to exhibit symptoms for a minimum of 9 months (vs the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition criterion of 6 months).

**Phase 2: Parent training**

The parent training phase was added to the protocol as a means of providing a more conservative approach to treating a vulnerable population of children with ADHD. Such an approach is consistent with guidelines specified by the AACAP to attempt a psychosocial intervention before preschoolers with ADHD are placed on medication (Dulcan, 1997). The parent training was based on the Community Parent Education (COPE) model developed by Cunningham and colleagues (Cunningham et al., 2000; Cunningham, Bremner, & Boyle, 1995; Cunningham, Bremner, & Secord, 1998). The intervention consisted of 10 weekly, 2-hour group sessions led by a parent trainer with similar qualifications as those in the NIMH MTA Study (Wells et al., 2000), namely, an ABD or PhD psychologist, or an experienced master’s-level clinician. Since screening did not occur at the same time for all families, some families had to wait longer than others from the time of screening to the beginning of parent training so that an adequate group size could be achieved. Sites were encouraged to allow screen failures the option of participating in parent training to increase the group size. If parents requested and clinicians agreed that patients were severely symptomatic, children could be moved directly into medication phase while completing the parent training phase.

**Phase 3: Baseline**

Beginning in week 8 of the 10-week parenting workshop, patients were scheduled
for Baseline assessment to determine continued symptomatology and eligibility to continue in the trial. Baselines assessment consisted of collection of both parent and teacher behavior rating scales, as well as ratings of impairment by parents, teachers, and an expert clinician. Specific a priori criteria for continued symptomatology and impairment were established to ensure that patients who showed improvement during the parent workshop were not unnecessarily exposed to medication.

If children were eligible to continue on the basis of these criteria, parents were reconsented to remind them of the risks and benefits of the medication phases that followed. This consent procedure at this and subsequent points in the study was designed to address another concern that was raised at the AACAP Research Forum on preschool psychopharmacology trials (Greenhill et al., 2003) that families of children in this age range who were participating in trials, such as the PATS, would not have their needs met fully in a single consent experience. The PATS was long and complex. As a result, both the Research Forum and the NIMH DSMB recommended that, when a child enters each new phase of the PATS, parents get a 1-page summary of what will occur. There needed to be a separate consent process at each phase focusing on the risk/benefit issues (and alternatives to stopping) for the final, discontinuation phase. In other words, families met with the investigators before each of the 8 phases of the study and were explicitly reconsented. Risks and benefits were discussed, as were other essential elements of consent (eg, confidentiality, voluntary nature of research/right to withdraw, etc).

**Phase 4: Open-label safety lead-in**

Phase 4 was designed to determine if patients could tolerate the doses of medication to be used in the double-blind phases of the protocol. A step-up open titration of methylphenidate was used, beginning with 1.25 mg BID and increasing to 7.5 mg TID by the end of 1 week. Adverse events were monitored throughout the week on an informal basis through telephone communication with the family. Children who showed moderate to prohibitive AEs at doses lower than 7.5 mg were not eligible to continue into the double-blind phase of the study. These patients, however, could be considered for entry into the open-label maintenance phase if there was evidence of tolerability at the lower doses (eg, 1.25 mg or 2.5 mg). Children who tolerated all doses except the 7.5-mg dose were eligible to enter the crossover titration phase under a modified schedule, wherein the 7.5-mg-dose week was substituted with a second 5-mg-dose week.

Safety concerns focused on dosing, because there was little consensus on the safe and effective dose of methylphenidate for very young children. Some studies had reported that preschool children get tearful, depressed looking, and “zombie like” on stimulants (Firestone et al., 1998). The PATS investigators had first recommended an MPH dose range from 2.5 mg TID to 10 mg TID. However, the NIMH DSMB recommended that the starting dose be 1.25-mg MPH 3 times daily. This is one-fourth the lowest commercially available MPH dose. This design change necessarily truncated the upper bound of medication efficacy that we were able to evaluate for this age range.

**Phase 5: Five-week double-blind, placebo-controlled, crossover-design, titration study**

All children who tolerated the dosing in phase 4 were eligible to enter the 5-week crossover titration trial. During this phase, each child was randomized to a sequence in which the following 5 drug conditions were switched on a weekly basis: placebo TID, 1.25 mg TID, 2.5 mg TID, 5 mg TID, and 7.5 mg TID. The active and placebo medication was provided in identical capsules. At the end of each week, information was obtained from teachers, parents and children, and included ratings of school and home functioning and side effects. The rating forms used in the MTA titration trial—the CLAM, the SKAMP, and Side Effect Forms—were used in this titration trial (Greenhill et al., 1996; Swanson et al., 1998).
At the end of the 5-week trial, each patient’s data for each of the 5 drug conditions was reviewed before breaking the blind to determine an individual’s best dose for phase 6. To maximize the reliability of this decision-making process, the following algorithm was applied. Teacher and parent ratings were individually graphed for each dose condition, and side effects tabulated. Using procedures worked out in the MTA Study (Greenhill et al., 1996) and later refined (Swanson et al., 2001), 2 clinicians (1 from the treating site, 1 from other sites) reviewed the graphed dose-response functions and side effect tables. The algorithm specified the exact procedures for rank ordering the various dosage points on the graphs, and what steps were taken to select the best dose, to identify a placebo responder (flat dose-response curve with no room for improvement) or identify an inadequate response. If the 2 clinicians disagreed, the best dose was subsequently resolved via consensus on a cross-site conference call.

Phase 6: Four-week, double-blind, placebo-controlled parallel study

This phase began by randomly assigning titration completers to either their best dose of methylphenidate or to a placebo condition. This trial lasted 4 weeks, with an efficacy assessment conducted at the end of the last (4th) week, using an average of parent and teacher ratings. The FDA recommended the addition of this phase to provide an additional, more definitive test of efficacy. This new phase was added to reduce concerns about possible carry over effects that often perturb crossover designs, such as the PATS 5-week crossover titration phase.

One additional design feature that was added to increase safety and ensure ethical treatment of all participants was especially salient during phase 6. Prompted, in part, by several individual site Institutional Review Boards, the PATS trial allowed patients and families who opted out of the controlled, double-blind phases to continue into the maintenance phase of the study. This greatly reduced any incentives for families to remain in the double-blind phases, especially if there was reason to suspect the child had been randomized to receive placebo.

Phase 7: Open-label maintenance

This phase was intended to provide systematic information, heretofore lacking, regarding the safety and relative long-term effectiveness of the MPH in 3- to 5-year-olds. Following phase 6, all patients were eligible to enroll into open-label treatment for 10 months. Procedures during open-label treatment were as follows. Each child’s starting dose in this phase was based on the best dose decision made at the end of phase 5. If deterioration occurred, the child’s dose was gradually titrated to an optimal dose. Maintenance treatment corresponded to the medication management procedures utilized in the MTA Study (Greenhill et al., 1996). Briefly, this included monthly clinic visits, during which information about the child’s functioning and side effects were obtained from the parent. In addition, prior to the first and last maintenance visit, teacher ratings of the child’s functioning and side effects were obtained from the parent. In review of this information, the pharmacotherapist adhered to clinical algorithms, developed and used in the MTA Study (Greenhill et al., 1996), to decide if any medication adjustments were warranted, including changes in dosage and/or timing of administration. Adherence to this common maintenance protocol by all pharmacotherapists was designed to reduce the likelihood of any site differences arising because of differences in treatment philosophy, dosing preferences, etc. A reassessment of child functioning occurred after 10 months of medication maintenance, prior to the placebo discontinuation trial.

Phase 8: Discontinuation

Following the phase 7 open-label treatment period with the MPH, a subset of patients was enrolled into a randomized, double-blind placebo discontinuation trial. The
discontinuation phase included an abrupt discontinuation in that half of the children were randomized to continue their best dose from end of maintenance and the other half of the children were placed on placebo without a taper. The transition to placebo occurred immediately upon entering the discontinuation phase. During this 6-week phase, information was obtained weekly from parents and teachers regarding patient functioning at home and at school. Children randomized to placebo were returned to active medication if they met a priori criteria for relapse.

Summary

In short, the PATS investigators made protocol modifications to ensure that preschool children entering the PATS underwent a thorough and detailed diagnostic procedure, had a severe form of the disorder, and had a prior trial of less-invasive parent training before any medication. Designing the PATS involved unique challenges, including the lack of information about the safest and most effective dose range for preschool children, how best to assess efficacy of the MPH, and the need to develop a rigorous, valid, reliable, definition of the ADHD that would be based on the reference range of behaviors and attention span in a 3-year-old child. These concerns are representative of those faced in conducting research and performing clinical practice with preschool children with ADHD. The remainder of the article is designed to interpret the findings from the extant literature and the lessons learned from the design of the PATS to provide recommendations for clinicians faced with the option of providing stimulant drug treatment for young children with ADHD.

GUIDELIENS CLINICIAN FOR STIMULANT USE IN PRESCHOOLERS WITH ADHD

Perhaps the most important guideline to note is that use of most stimulant products in children younger than 6 years is not indicated and is therefore considered off-label use. As such, clinicians should be cautious about initiating psychopharmacological treatment with preschool-aged children.

Both the AACAP and the American Academy of Pediatrics (AAP) have published guidelines that provide some direction for clinicians faced with managing preschool children with ADHD (Dulcan & Benson, 1997; AAP, 2001; Dulcan, 1997). These guidelines and their application to clinical practice are summarized by Kratochvil, Greenhill, March, Burke, and Vaughan (2004). For example, the AACAP recommends that treatment for the ADHD in this age range begin with some form of behavioral intervention, because this approach has been shown to be efficacious in treating the ADHD in preschoolers (Pisterman et al., 1989; Sonuga-Barke, Daley, Thompson, Laver-Bradbury, & Weeks, 2001). AACAP guidelines also recommend that children be placed in structured preschool settings prior to initiating medication. AAP guidelines, while not specific to preschool-aged children, similarly recommend the use of behavioral therapy and emphasize the need to identify specific individualized impairments that can be assessed as treatment targets.

If psychosocial interventions are unavailable or ineffective, both the AACAP and the AAP recommend a closely monitored trial with stimulant medication. The AACAP specifically recommends such a trial only for those cases that are more severe. Recommendations for dosing are to begin low and use a forced dose titration to determine optimal response to the medication while minimizing side effects. Both efficacy and adverse events should be monitored frequently in an objective manner. Once an optimal dose is identified, practice guidelines recommend that treatment proceed 7 days/wk and that children be seen for re-evaluation every 3 to 6 months.

At present, the recommendations for clinical use of stimulant medications in preschoolers with ADHD are little more than what would be intuitively deduced from good clinical practice guidelines. This lack of specific guidance is due, in part, to the state of
working with this population will limit the efficacy and tolerability of stimulant drugs for use in this highly vulnerable population. Large-scale research has been started (ie, the PATS trial), although ethical and practical challenges for working with this population will limit the rate of progress in understanding stimulant safety and efficacy for young children. While clinicians seem to prescribe more and more medication to children in this age range, they should be wary of the risks and adhere to what meager guidelines are currently available. In the next 12 to 24 months, we will have more data available from the PATS that will hopefully help to more specifically tailor treatment strategies for preschool children with ADHD.

REFERENCES


