

Assessment and Treatment of Attention-Deficit/Hyperactivity Disorder: Part 2

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood. In part 1 of this article, information regarding primary care assessment of ADHD was presented. Part 2 focuses on best practice guidelines for treatment once the diagnosis has been established. For most children, successful treatment of ADHD requires a multicomponent approach comprised of patient and family psychoeducation, use of medications approved by the US Food and Drug Administration (eg, stimulants) and/or behavioral interventions, and management of any psychiatric comorbid conditions. Furthermore, as ADHD is a chronic illness, primary care physicians will need to frequently reassess their patients and make treatment adjustments as needed. [*Pediatr Ann.* 2015;44(4):160-168.]



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Part 1 of this article addressed key components involved in the evaluation of attention-deficit/hyperactivity disorder (ADHD) in primary care settings. Part 2 provides information regarding evidence-supported treatments for this condition. Once the diagnosis has been established, the primary care provider (PCP) will want to begin the treatment planning process by discussing the diagnosis and treatment options with the patient and family. To best match treatment rec-

ommendations to the needs of the child, a number of unique factors need taken into consideration, including the patient's age, severity of illness, family preferences, and the availability of community resources.

TREATMENT

ADHD is a chronic illness and is best managed using a "medical home" model.^{1,2} Once a diagnosis has been made, the PCP should collaborate with the child and the family to formulate a comprehensive

individualized treatment plan. This plan should take into account patient and family preferences regarding types of treatment preferred and should be responsive to the unique individual, family, and environmental characteristics associated with the clinical presentation.

Initial treatment planning should include psychoeducation regarding the biological basis of ADHD, discussion of core symptoms and level of functional impairment, identification of additional care team participants (eg, teachers), an explanation of potential treatment modalities and how they will be implemented and monitored, and a discussion of the importance of periodic adjustments to the treatment plan as the developmental needs of the youth evolve.³

Although comprehensive treatment includes a number of possible interventions, the essential components of evidenced-based ADHD treatment involve medication management, parent and/or classroom behavioral interventions, or a combination of both. According to the American Academy of Pediatrics (AAP) and the American Academy of Child and Adolescent Psychiatry (AACAP) guidelines, the PCPs decision regarding which of these three modalities should be employed will depend on the youth's age, degree of impairment, availability of treatment resources, and patient and family preferences regarding the acceptability of the recommended treatments.

For preschool children (ages 4–5 years), if not already implemented, the PCP should recommend a course of evidence-based, parent- and/or classroom-based behavioral treatment. However, evidence-based behavioral interventions are not always available, and even when they are available they do not always lead to adequate reduction of symptoms, even after a suitable trial. In such cases, but only when the child's ongoing functional impairment is assessed to be in the moderate to severe range, the AAP recommends that a trial of methylphenidate may be appropriate. Indicators of moderate to severe dysfunction, in addition to a

failed trial of behavioral therapy, include ongoing ADHD symptoms of 9 months or more and functional impairment at home and at least in one more setting, such as at preschool.⁴ If medication is considered, the PCP should discuss with the parent(s) the risks of starting a medication compared with the risks of delaying treatment.²

For school-aged children (ages 6–11 years) and for adolescents (ages 12–18 years), the AAP guidelines indicate that the preferred treatment for ADHD comprises a US Food and Drug Administration (FDA)-approved ADHD medication, and an evidence-based parent and/or classroom behavioral intervention. For school-aged children, it is also reasonable to undertake either a medication trial or a behavioral intervention alone, although for adolescents, current evidence indicates behavior interventions alone to be inferior compared to combined treatment or medication alone. For adolescents, gaining patient assent to treatment and screening for substance use should be undertaken prior to initiating treatment.

For youth who present with clear evidence of functional impairment due to symptoms of inattention, hyperactivity, or impulsivity but who do not meet the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (*DSM-5*) criteria for an ADHD diagnosis, behavioral interventions, but not medications, can be recommended.²

Regardless of the mode of treatment, PCPs should have a system in place to monitor response to treatment both in terms of expected benefits and potential negative effects.⁵ Assuming baseline symptoms and functional status have been quantified prior to treatment, follow-up rating scales can be obtained from parents, teachers, and others periodically to track symptom and functional change over time. In addition to documenting baseline symptoms, it is important to gather information regarding the patient's current daily routines, ability to engage in expected behaviors (eg, chores), other health concerns such as sleep, mood,

TABLE 1.

Behavioral Management Suggestions

- Help parents increase structure, predictability, and consistency at home
- Review child's daily schedule with parents to screen for inappropriate activities or inadequate levels of supervision; provide recommendations if necessary (eg, supervised day camps during the summer)
- Discuss and model clear and specific caregiver communication skills
- Establish realistic and observable parent behavioral expectations for their child
- Increase parent focus on rewarding desirable behaviors ("catch them being good")
- Ignore annoying or attention-seeking behaviors
- Use appropriate discipline (eg, loss of privileges) in a consistent, predictable, and immediate way
- Promote improvement of parent-child relationships by "prescribing" daily child-directed play time with parent

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or appetite issues, and current parental level of functioning in order establish reasonable expectations for treatment and to avoid misattributing baseline characteristics to unwanted treatment effects.^{6,7}

Behavioral Interventions

There are substantial data to support evidence-based behavioral interventions for ADHD.^{8,9} Primary care providers generally will not have the time or expertise to implement formal behavioral interventions during office visits but should be aware of some of the basic goals and principles of behavioral management training (BMT), which can be included as part of the psychoeducational process. **Table 1** lists a number of behavioral management suggestions that clinicians might find helpful.

In terms of formal interventions, a large number of programs are available, many of which have been systematically studied.⁹ Programs with well-established evidence for their efficacy include Parent-Child

Interactive Therapy (PCIT), The Incredible Years Program, and Triple P (Positive Parenting Program).¹⁰ BMT enhances behavioral regulation through targeting maladaptive parent-child interaction patterns and teaching behavioral strategies that provide children with direct and immediate consequences for both their desirable and undesirable behaviors. Parents are taught how to observe, identify, and record discrete child behaviors, and are instructed on how to communicate their behavioral expectations clearly, calmly, and effectively. An emphasis is placed on learning to apply appropriate consequences in a consistent and timely fashion to help their child with adaptive functioning. BMT uses both positive reinforcement for desired behaviors and punishment (eg, timeout) for undesired behaviors, but there is a clear bias toward positive reinforcers, such as praise, contingent rewards (eg, token economies), and selective parental attention for appropriate behaviors.

BMT for ADHD differs from standard BMT for disruptive behaviors in several ways. First, parents are taught to look at their child's disruptive behaviors through the lens of ADHD to better understand that their child's behavioral problems are a function of their biological impairment and are not done willfully out of spite or to undermine their role as parents. Once parents come to understand that children with ADHD have significant deficits in their ability to internally monitor and regulate their behaviors (eg, through self-talk, anticipating consequences, or accessing prior learning), they will be in a better position to help their child improve his or her functioning. Second, compared to children without ADHD, children with ADHD may need more support from their parents in helping promote self-regulation through giving ongoing feedback regarding their behaviors. Third, children with ADHD often do not respond to typical reward cues (eg, a smiley face from a teacher or praise for staying on task) that might reinforce a child without ADHD. Thus, parents will

have to work hard to find relevant salient rewards that capture their child's attention and are experienced as meaningful in order to shape his or her behavior in positive ways. Lastly, consequences for behavior (both negative and positive) need to be immediate, as potential rewards or negative consequences positioned too far out in the future may lack the saliency to influence current behaviors (Personal communication, Erin N. Schoenfelder, PhD, October 2, 2014).

Limitations

In the Multimodal Treatment Study of Children with ADHD (MTA) study,⁴ the initial findings indicated that medication treatment alone and combination treatment were superior to BMT alone and community treatment, but combination treatment was no better than medication alone for treating core symptoms of ADHD. However, combined treatment had better outcomes in a number of secondary measures, including for parent-child interactions, reading achievement, teacher-rated social skills, and internalizing symptoms such as anxiety.⁴ As discussed above, at the 8-year naturalistic follow-up to the initial MTA study, the original differences among the four treatment groups had dissipated.¹¹ A recent analysis of commercially insured youth with ADHD indicated that of a sample of more than 300,000 youth with ADHD receiving medications, only one-quarter had received any type of concurrent therapy in the previous year.¹² These findings stress the importance of the PCP periodically reassessing the need for their patients and families to re-engage in psychosocial services, such as BMT, as youth with ADHD transition into adolescence and their developmental needs change. Also, the PCP needs to be aware that parental factors such as parental ADHD, substance use, or family discord may affect a parent's ability to learn and apply the skills taught in BMT.⁷ A final challenge is that, whether applied in the home or in the school setting, the gains from BMT may be

difficult to generalize to other community settings where intensive adult support may be lacking.³

Working with Schools

Programs that apply behavioral classroom management strategies are also available at many schools and have been found to provide moderate-to-large benefits in nonrandomized studies.¹³ Students with ADHD may qualify for classroom accommodations in the form of a 504 plan or individualized education program under the classification of "other health impairment" if it is found that the disorder is having a negative impact on academic or behavioral functioning.¹⁴ Typical services provided include modified classroom and homework assignments, preferred seating, and extended time to complete tests. Primary care providers may need to help parents advocate for such services and can help their patients succeed in school through ongoing communication with teachers and other school personnel regarding the child's response to school-based interventions. Use of a daily report card and obtaining periodic follow-up ADHD rating scales can be helpful in tracking school progress.³

Medications

AAP and AACAP guidelines recommend that medication management for ADHD begin with a medication approved by the FDA. The exception to this is the recommendation from the AAP that methylphenidate should be prescribed in place of dextroamphetamine in preschool children, because although dextroamphetamine is approved for this age range, there is more evidence for the efficacy and safety of methylphenidate.

Three classes of medications currently have FDA approval for the treatment of ADHD in youth: (1) stimulants, (2) one selective norepinephrine reuptake inhibitor (atomoxetine), and (3) two alpha-adrenergic agonists. Of the three classes, the stimulants have been shown to have the greatest effect size (approximately 1.0), whereas

TABLE 2.

Dosing Guidelines for FDA-Approved Stimulant Medications

Medications	Initial Starting Dose	Typical Frequency	Onset of Action	Duration (hours)	FDA Maximum Daily Dose	Available Doses	Comments
Methylphenidate (MPH) class							
Methylphenidate	5 mg bid	bid-tid	20-60 minutes	4-6	60 mg	5, 10, 20 mg tablets	Half dose if ages 3-5 years; liquid and chewable tablets also available
Dexmethylphenidate	2.5 mg bid	bid	20-60 minutes	4-6	20 mg	2.5, 5, 10 mg tablets	Half dose if ages 3-5 years
OROS methylphenidate	18 mg qam	qd	20-60 minutes	10-12	72 mg	18, 27, 36, 54 mg capsules	Osmotic capsule
Biphasic release 30/70	20 mg qam	qd	20-60 minutes	4-6	60 mg	10, 20, 30, 40, 50, 60 mg capsules	Beads in capsule can be sprinkled
Methylin ER Methylphenidate SR Methylphenidate hydrochloride ER	10 mg qam	qd-bid	60-180 minutes	4-6	60 mg	10, 20 mg tablets	Uses wax matrix; variable duration of action
Biphasic release 50/50	20 mg qam	qd	20 to 60 minutes	6-8	60 mg	10, 20, 30, 40 mg capsules	Beads in capsule can be sprinkled
Dexmethylphenidate XR	5 mg qam	qd	20-60 minutes	10-12	30 mg	5, 10, 15, 20 mg capsules	Beads in capsule can be sprinkled
MPH transdermal patch	10 mg qam	qd	60-120 minutes	9	30 mg	10, 15, 20, 30 mg (maximum 30 mg per 9 hours)	Patch continues working up to 2 hours after removed
Methylphenidate ER liquid	20 mg qam	qd	45 minutes	8-12	60 mg	5 mg/mL liquid	No generic available
Amphetamine class							
Mixed amphetamine salts	2.5-5 mg qd	bid-tid	20-60 minutes	4-6	40 mg	5, 7.5, 10, 12.5, 15, 20, 30 mg tablets	Half dose if ages 3-5 years
Dextroamphetamine, short-acting	2.5-5 mg qd to bid	bid-tid	20-60 minutes	4-6	40 mg	2.5, 5, 7.5, 10, 20, 30 mg tablets	FDA-approved for ages 3-5 years
Mixed amphetamine salts, biphasic release 50/50	5 mg qd	qd	20-60 minutes	8-12	40 mg	5, 10, 15, 20, 25, 30 mg capsules	Beads in capsule can be sprinkled
Dextroamphetamine, extended release	5 mg qd	qd-bid	≥60 minutes	≥6	60 mg	5, 10, 15 mg capsules	Also approved for the treatment of narcolepsy
Lisdexamfetamine	30 mg qd	qd	60 minutes	10-12	70 mg	20, 30, 40, 50, 60, 70 mg capsules	Beads in capsule can be sprinkled; no generic available

Abbreviations: bid, twice per day; ER, extended release; FDA, US Food and Drug Administration; GI, gastrointestinal; qam, every day before noon; qd, four times per day; SR, sustained release; tid, three times per day; XR, extended release.

Adapted from Pierce.³

both atomoxetine and the approved alpha agonists have an effect size of approximately 0.7.¹⁵

Stimulants: Stimulants are generally preferred as the initial medication of choice. Comprised of two types, methylphenidate-based and amphetamine-based, they can be highly effective in treating the core symptoms of ADHD.¹⁶ It is estimated that 65% to 75% of children will have a favorable clinical response to an initial trial to either methylphenidate or amphetamine.¹⁷ An even higher response rate can be obtained (estimated to be 85%) if the PCP provider switches types in initial nonresponders, as some youth show preferential response to one of the types.¹⁸ Typical starting doses, maximum recommended dose, and other pertinent clinical information is provided in **Table 2**. In the MTA study, the mean optimal dose of methylphenidate was approximately 1 mg/kg, and children in the combined treatment program were able to be stabilized on lower total daily doses compared to children treated with medication alone.

Although maximum dose and weight-based guidelines are clinically useful, each patient will have their own unique dose-response curve and side effect profile; therefore, in certain cases, the clinician may need to raise the dose beyond FDA limits, especially in some adult-sized adolescents.¹⁷ In general, the goal of titration should be to find the dose of medication that maximizes functional improvement with the minimal amount of side effects.^{14,17} In young children, clinicians often prefer to start a short-acting stimulant due to safety concerns and perceived greater ease of titration to an effective dose. However, to achieve adequate symptom coverage, short-acting agents need to be taken two to three times a day, which can lead to problems with adherence and inconsistent timing of dosing. The need for in-school dosing can be especially problematic for older youth, who often-times are reluctant to take medications at school due to privacy concerns. Therefore, in general, long-acting preparations are

recommended to promote adherence and to avoid unnecessary logistical complications. The exception would be for children who weigh less than 16 kg, as there are few long-acting formulations available at a sufficiently low-starting dose.¹⁷

Once started, clinicians (or designated office staff) should frequently obtain parent and teacher feedback verbally or through rating scales to monitor efficacy and to identify any adverse effects. Recommendations regarding the length of time between titration range from 3 days to 3 weeks,^{14,17} but in general, it is probably wise to leave a child on a selected dose for at least 1 week before obtaining feedback from informants regarding the stimulant's effectiveness. During this titration process, it will be important to schedule monthly office visits to monitor for side effects and track weight, height, pulse rate, and blood pressure. Frequent office visits also provide the opportunity to continue patient and family psychoeducation regarding ADHD, address any concerns, and help the family come to understand that adequate management of ADHD is an ongoing process. Once an effective dose is found, office visits can occur less regularly, such as on a quarterly or semi-annual basis. However, as mentioned above, as the child's development continues, new environmental challenges and functional expectations may necessitate treatment plan changes, including changes in medication or other nonmedication interventions.

Preschool-aged Children: Results from the Preschool ADHD Treatment Study (PATS)¹⁹ found that for children ages 3 to 5 years with severe ADHD who were unresponsive to a 10-week behavioral management intervention, treatment with methylphenidate was an effective intervention for their ADHD symptoms. However, compared with older children receiving methylphenidate, mean optimal dose (approximately 0.7 mg/kg) and effect sizes were lower. Also, compared with the MTA study, there were more reported sleep and appetite problems and emotionally related

events, such as crying, irritability, and crab-biness, particularly at higher dose ranges. These results suggest that for preschool children with moderate to severe ADHD, methylphenidate treatment should begin at lower doses (eg, 2.5 mg twice a day) and should be titrated more slowly and in smaller increments than in older children.

Adolescents: As discussed above, adolescents with ADHD may display fewer symptoms of hyperactivity and impulsivity than younger children, have different developmental challenges compared with younger children, and are at greater risk for substance abuse than younger children. Particular attention should be paid to identifying specific targets for treatment that are pertinent for the adolescent's evolving functional demands. For example, if a teen drives, it is important consider providing medication treatment for symptom control throughout the day into the evening. Adolescents with ADHD, compared to youth without ADHD, are at fourfold greater risk of developing substance abuse problems.²⁰ If substance abuse is present, it should be treated prior to initiating a stimulant trial; if this is not achievable, then nonstimulant alternatives should be chosen. Additionally, adolescents are also at greater risk for diverting stimulants and/or using them for as performance agents (eg, staying up all night to study for a test). Therefore, the PCP should be ready to carefully monitor for any signs of misuse.

Common side effects of stimulants include appetite suppression, weight loss, insomnia, headaches, and abdominal pain. Encouraging healthy eating habits for breakfast and after the medication wears off in the evening can prevent weight loss.³ Even when untreated, children with ADHD are more likely to have sleep disturbances compared to children without ADHD, so it important to obtain a thorough sleep history prior to initiating treatment.²¹ Adolescents, especially, should be monitored for delayed sleep phase syndrome, which may occur with stimulant treatment.²⁰ Factors that increase the risk of stimulant-induced

TABLE 3.

Dosing Guidelines for FDA-Approved Nonstimulant Medications

Medications	Initial Starting Dose	Typical Frequency	Time to Benefit	Duration (hours)	FDA Maximum Daily Dose	Available Doses	Comments
Atomoxetine	0.5 mg/kg per day, then increase to 1.2 mg/kg per day	qd-bid	1-2 weeks	10-12	1.4 mg/kg	10, 18, 25, 40, 60, 80, 100 mg (capsules)	May have GI side effects; may take 6 weeks for full benefit
Clonidine, extended release	0.1 mg qd	qd-bid	1-2 weeks	10-12	0.4 mg/day	0.1, 0.2 mg (tablets)	Also approved by FDA as adjunct to stimulants; often used for sleep and to treat tics
Guanfacine, extended release	1 mg/d	qd	1-2 weeks	10-12	7 mg/day (weight based)	1, 2, 3, 4 mg (tablets)	Also approved by FDA as adjunct to stimulants; often used for sleep and to treat tics

Abbreviations: bid, twice per day; FDA, US Food and Drug Administration; GI, gastrointestinal; qd, four times per day. Adapted from Pierce.³

sleep disturbance include young age, being stimulant-naïve, and being on higher doses of stimulants.²² Less common side effects include affective flattening, irritability, mood lability, tics, and medication “rebound,” which is often reported as increased restlessness, irritability, and noncompliance when the stimulant wears off. Rebound may be a result of reappearance of ADHD symptoms as the stimulant wears off, and it is sometimes successfully treated with a small dose of a short-acting stimulant.²³ The above side effects, if present, are often transient, and therefore the patient and family should be encouraged to continue treatment as long as they can be tolerated and do not pose a health risk. If problems persist, however, it may be necessary to decrease the dose or consider an alternative stimulant.¹⁷

Extensive research has been undertaken to determine whether or not stimulants (especially when concurrently prescribed with alpha agonists) increase the risk for serious cardiovascular events, such as sudden cardiac death. Although extremely rare, several large studies have indicated that there may be a doubling of such risk compared with nonusers.^{24,25} Therefore, before starting a stimulant, PCPs should inquire about any patient history of structural heart defects, hypertrophic cardiomyopathy, arrhythmias (eg, prolonged QT syndrome), or sudden death in family members, especially at a

young age. Questions should also be asked regarding any patient history of chest pain, syncope, exercise intolerance, or palpitations. If concerns are present, the patient should be referred for a cardiac evaluation prior to starting a stimulant. However, in the absence of such concerns, routine pretreatment electrocardiogram screening is not recommended.^{14,17,26} Blood pressure and pulse should also be regularly monitored, as stimulant use is also rarely associated with significant elevations in these measures of cardiac function.

Psychotic symptoms (especially tactile and visual hallucinations of insects) and mania have also rarely been reported with stimulant use, and therefore the PCP should monitor for them.¹⁷ Additionally, parents often raise concerns regarding the effects of long-term stimulant use on growth. The MTA study reported diminished growth velocity occurred during (but not beyond) the first 3 years of treatment, leading to a loss of 1 to 2 cm of growth. However, a more recent longitudinal study found no associations between use of stimulant medication and changes to predicted growth or adult height.²⁷

Atomoxetine: Although associated with a lower effect size than the stimulants, atomoxetine can be considered as the initial treatment choice in a number of clinical situations. First, several clinical guidelines recommend atomoxetine as a

first-line option for children with ADHD and co-occurring anxiety, as it may lead to improvement in both conditions.²⁸ Second, because atomoxetine carries no risk for abuse or dependence, it is preferred over stimulants for youth with ongoing substance abuse problems or who are at risk for stimulant diversion or performance enhancement use. Third, for a variety of reasons, families may not be willing to have their children take a stimulant. Finally, atomoxetine is also reasonable choice for children who do not respond to stimulants or who experience intolerable side effects on stimulants, such as extreme irritability or impairing tics.

Atomoxetine may be given once daily or twice daily. Twice daily dosing may increase tolerability and improve symptom coverage throughout the day. (For dosing information, see **Table 3**.) Although studies show that atomoxetine separates from placebo as early as 1 week into treatment, full therapeutic effects may take up to 6 weeks to be realized, which suggests that compared with stimulants, more time will be required to properly gauge clinical efficacy at a given dose of medication.¹⁷

Common side effects of atomoxetine include stomach complaints such as nausea, decreased appetite, dizziness, sleep disturbance, headache, and fatigue. There are several serious potential side effects associated with atomoxetine, which should

be discussed with patients and families prior to initiating treatment. Based on data from several pooled studies comparing atomoxetine to placebo, atomoxetine received a black box warning for increased suicidal ideation. Therefore, patients should be carefully monitored for any signs of increased suicidal thinking or worsening clinical status, especially when initiating treatment or undergoing dose changes. Patients taking atomoxetine should also be monitored for jaundice as there have been rare reports of acute hepatic failure in patients taking atomoxetine, although at this time routine monitoring of hepatic functioning is not recommended.¹⁷ Finally, as with stimulants, there have been reports of sudden cardiac death in patients with significant heart disease taking atomoxetine, so a careful cardiac history and physical exam needs to be undertaken prior to initiating treatment.

Alpha agonists: Both extended-release guanfacine and clonidine (**Table 3**) have been shown to have efficacy in the treatment of ADHD, and they now have FDA approval for use both as monotherapy and for adjunctive therapy (augmentation to stimulants) in children with ADHD. Adjunctive therapy is most commonly undertaken in patients who have shown a partial response to stimulants but are unable to tolerate them at higher doses. As monotherapeutic agents, the extended-release alpha agonists show comparable efficacy to atomoxetine. Full therapeutic effect at a given dose may take up to 4 weeks.

Common side effects include somnolence, headache, fatigue, dizziness, abdominal pain, and more rarely hypotension. If somnolence is a concern, dosing can occur before bed. Due to the potential for hypotension, blood pressure should be monitored routinely, especially during dose changes. Parents should be warned of the potential for rebound hypertension if the medication is stopped abruptly. Studies in the 1990s raised concerns about the use of alpha agonists (especially immediate-release clonidine) in conjunction with

stimulants due to a number of reports of significant heart rate changes following dose adjustments and the deaths of four children taking clonidine and methylphenidate.¹⁷ Although no clear causative relationship has ever been established linking the deaths to combination treatment, clinicians should routinely monitor heart rate and ask questions about dizziness, fainting, or unexplained changes in cardiac function. Also, because the alpha agonists have a fairly narrow therapeutic window and are sometimes used to regulate sleep, PCPs should caution parents not to increase the dose of an alpha agonist prior to discussing this plan with their provider.

Non-FDA-approved Medications:

Immediate-release clonidine and guanfacine have long been used off-label in children with ADHD to treat symptoms of ADHD, control side effects such as tics and insomnia, and to reduce comorbid symptoms such as irritability or aggression. Although generally used as adjunctive therapy to stimulant treatment, effect sizes as high as 0.58 have been reported.¹⁷ As with the long-acting agents, both clonidine and guanfacine need to be gradually titrated during the initiation phase of treatment and gradually tapered when discontinued. Side effect profiles are similar to their related extended-release versions. Bupropion also has been shown to have efficacy for ADHD in open-label trials in adults and adolescents. Like all antidepressants, it carries a black box warning regarding the potential for increased suicidal ideation in youth and young adults. It is contraindicated in patients with seizure disorder.

Treating Comorbid Conditions

Comorbid conditions are commonly either present at the time of ADHD diagnosis or emerge at some point in treatment. Depending on the comorbid condition and its level of severity, the PCP may feel comfortable providing treatment for the associated condition, or alternatively, may need to refer the child to a specialist.

The Texas Children's Medication Algorithm Project (TCMAP)²⁸ has published algorithms that can help guide treatment for ADHD and several other common comorbid conditions. Each algorithm provides the option for nonmedication interventions. In terms of medication interventions, the anxiety algorithm provides the option to begin treatment with a stimulant or atomoxetine. If ADHD symptoms improve but anxiety persists, an SSRI may be subsequently tried. When major depression co-occurs with ADHD, the TCMAP authors recommend treating the more severe disorder first and subsequently considering treatment for the less severe disorder if symptoms persist. For ADHD and associated tic disorders, if stimulant treatment fails to treat or exacerbates a tic disorder, the addition of an alpha agonist may be a reasonable next step if there is significant functional impairment. Both oppositional defiant disorder (ODD) symptoms and aggression, when co-presenting with ADHD, may improve following optimized stimulant treatment but should not be prescribed for these symptoms in the absence of ADHD.²⁹ However, for youth who present with ADHD and conduct disorder (CD), consensus guidelines recommend treatment with nonstimulant medications (eg, atomoxetine), given the increased risk for stimulant diversion in this population.³⁰ Youth who present with comorbid ODD or CD show greater overall impairment and have a worse prognosis than youth with ADHD only and will likely require intensive, ongoing mental health services. Sleep disturbances occur at an increased rate in youth with ADHD and may worsen with stimulant and nonstimulant treatment.²¹ When sleep disturbances are considered significant and sleep hygiene measures fail to produce significant improvement, treatment with sleep aides, such as antihistamines, alpha agonists, melatonin, or trazodone, can be considered.¹⁷ However, all of these medications have the potential to produce worrisome side effects, which may limit their usefulness. For a number

of other comorbid conditions, such as autism and pediatric bipolar disorder, the PCP may feel more comfortable referring the patient to a specialty provider for further assessment and stabilization prior to providing ongoing treatment.

Alternative Treatments

A number of alternative treatments have been developed to treat ADHD, some of which have been systematically studied. Of those studied, omega-3 fatty acid supplementation, elimination of food colorings, and other elimination diets have the best evidence for efficacy but are likely to only be a viable option for a subset of patients.³¹⁻³³ Other alternative interventions such as neurofeedback, use of megavitamins, and chelation therapy currently have insufficient evidence to support their use, and in the case of megavitamins and chelation therapy, may cause adverse health consequences and therefore are contraindicated.³⁴

Ongoing Care

ADHD is a chronic condition and a substantial number of youth will continue to need treatment into adulthood. However, some youth may no longer need medication treatment as they grow older. If a parent reports no significant change in their child's function while off his or her medication (eg, during a medication holiday) or there has been, despite significant growth or increase in developmental demands, no need to adjust a youth's dose of medication for a considerable period of time, a trial off the medication may be warranted. If undertaken, care should be given to avoid conducting a medication-free trial during certain times, such as at the beginning of the school year or when increased functional demands or stressors are present.^{3,17} Prior to initiating the trial, current symptoms, functioning, and side effects should be quantified so that any changes that occur while the patient is not taking medicine can be adequately measured.

CONCLUSION

ADHD is a common, and oftentimes chronic, childhood condition frequently encountered in primary care settings. PCPs should feel confident in their abilities to provide comprehensive treatment for this disorder once a diagnosis has been established. Through partnering with the patient, family members, and other important adults in a child's life, a PCP can develop and initiate a multicomponent treatment plan that best fits the child's needs. Best practice ADHD treatment guidelines recommend psychoeducation, medication and/or behavioral interventions, and treatment of comorbid conditions as the most effective interventions. Because ADHD is frequently a chronic condition and symptom presentations may change with time, PCPs will need to periodically reassess their patients and make changes as needed.

REFERENCES

1. Feldman HM, Reiff MI. Clinical practice. Attention deficit-hyperactivity disorder in children and adolescents. *N Engl J Med*. 2014;370(9):838-846.
2. Larson K, Russ SA, Kahn RS, et al. Patterns of comorbidity, functioning, and service use for US children with ADHD, 2007. *Pediatrics*. 2011;127:462-470.
3. Pierce K. Treatment of attention-deficit/hyperactivity disorder. *Pediatr Ann*. 2011;40(11):556-562.
4. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of Children with ADHD. *Arch Gen Psychiatry*. 1999;56(12):1073-1086.
5. Barkley RA, Murphy KR. *Attention Deficit Hyperactivity Disorder: A Clinical Workbook. A collection of Rating Scales, Handouts, and Instructions for Clinicians, Parents, and Teachers*. 3rd ed. New York, NY: Guilford Press; 2006.
6. Warikoo N, Faraone SV. Background, clinical features and treatment of attention deficit hyperactivity disorder in children. *Expert Opin Pharmacother*. 2013;14(14):1885-1906.
7. Chronis AM, Chacko A, Fabiano GA, Wymbs BT, Pelham WE Jr. Enhancements to the behavioral parent training paradigm for families of children with ADHD: review and future directions. *Clin Child Fam Psychol Rev*. 2004;7(1):1-27.
8. Daley D, van der Oord S, Ferrin M, et al.; European ADHD Guidelines Group. Behavioral interventions in attention-deficit/hyperactivity disorder: a meta-analysis of randomized controlled trials across multiple outcome domains. *J Am*

- Acad Child Adolesc Psychiatry*. 2014;53(8):835-847.
9. Pelham WE Jr, Fabiano GA. Evidence-based psychosocial treatments for attention-deficit/hyperactivity disorder. *J Clin Child Adolesc Psychol*. 2008;37(1):184-214.
10. Eyberg SM, Nelson MM, Boggs SR. Evidence-based psychosocial treatments for children and adolescents with disruptive behavior. *J Clin Child Adolesc Psychol*. 2008;37(1):215-237.
11. Molina BS, Hinshaw SP, Swanson JM, et al.; MTA Cooperative Group. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *J Am Acad Child Adolesc Psychiatry*. 2009;48(5):484-500.
12. Gellad WF, Stein BD, Ruder T, et al. Geographic variation in receipt of psychotherapy in children receiving attention-deficit/hyperactivity disorder medications. *JAMA Pediatr*. 2014;168(11):1074-1076.
13. DuPaul G, Eckert T, Vilaro B. The effects of school-based interventions for attention deficit/hyperactivity disorder: a metaanalysis 1996-2010. *School Psychol Rev*. 2012;41:387-412.
14. Subcommittee on Attention-Deficit/Hyperactivity Disorder; Steering Committee on Quality Improvement and Management, Wolraich M, Brown L, Brown RT, et al. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics*. 2011;128(5):1007-1022.
15. Newcorn J, Kratochvil CJ, Allen AJ, et al. Atomoxetine and osmotically released methylphenidate for the treatment of attention deficit hyperactivity disorder: acute comparison and differential response. *Am J Psychiatry*. 2008;165(6):721-730.
16. Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Jacobsen SJ. Modifiers of long-term school outcomes for children with attention-deficit/hyperactivity disorder: does treatment with stimulant medication make a difference? Results from a population-based study. *J Dev Behav Pediatr*. 2007;28(4):274-287.
17. Pliszka S; AACAP. Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2007;46(7):894-921.
18. Arnold LE. Methylphenidate vs. amphetamine: comparative review. *J Atten Disord*. 2000;3:200-211.
19. Greenhill L, Kollins S, Abikoff H, et al. Efficacy and safety of immediate-release methylphenidate treatment for preschoolers with ADHD. *J Am Acad Child Adolesc Psychiatry*. 2006;45(11):1284-1293.
20. Mannuzza S, Klein RG, Bessler A, Malloy P, LaPadula M. Adult outcome of hyperactive boys. Educational achievement, occupational rank, and psychiatric status. *Arch Gen Psychiatry*. 1993;50(7):565-576.
21. Stein MA, Weiss M, Hlavaty L. ADHD treat-

- ments, sleep, and sleep problems: complex associations. *Neurotherapeutics*. 2012;9(3):509-517.
22. Santisteban JA, Stein MA, Bergmame L, Gruber R. Effect of extended-release dexamethylphenidate and mixed amphetamine salts on sleep: a double-blind, randomized, crossover study in youth with attention-deficit hyperactivity disorder. *CNS Drugs*. 2014;28(9):825-833.
 23. Swanson JM, Wigal S, Greenhill LL, et al. Analog classroom assessment of Adderall in children with ADHD. *J Am Acad Child Adolesc Psychiatry*. 1998;37(5):519-526.
 24. Cooper WO, Habel LA, Sox CM, et al. ADHD drugs and serious cardiovascular events in children and young adults. *N Engl J Med*. 2011;365(20):1896-1904.
 25. Dalsgaard S, Kvist AP, Leckman JF, Nielsen HS, Simonsen M. Cardiovascular safety of stimulants in children with attention-deficit/hyperactivity disorder: a nationwide prospective cohort study. *J Child Adolesc Psychopharmacol*. 2014;24(6):302-310.
 26. Perrin JM, Friedman RA, Knillans TK; Black Box Working Group; Section on Cardiology and Cardiac Surgery. Cardiovascular monitoring and stimulant drugs for attention-deficit/hyperactivity

- disorder. *Pediatrics*. 2008;122(2):451-453.
27. Harstad EB, Weaver AL, Katusic SK, et al. ADHD, stimulant treatment, and growth: a longitudinal study. *Pediatrics*. 2014;134(4):e935-e944.
 28. Pliszka SR, Crismon ML, Hughes CW, et al. Consensus Conference Panel on Pharmacotherapy of Childhood Attention Deficit Hyperactivity Disorder. The Texas Children's Medication Algorithm Project: revision of the algorithm for pharmacotherapy of attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2006;45(6):642-657.
 29. Matthys W, Lochman JE. *Oppositional Defiant Disorder and Conduct Disorder in Childhood*. West Sussex, UK: John Wiley & Sons Ltd.; 2010:159-166.
 30. Kutcher S, Aman M, Brooks SJ, et al. International consensus statement on attention-deficit/hyperactivity disorder (ADHD) and disruptive behaviour disorders (DBDs): clinical implications and treatment practice suggestions. *Eur Neuropsychopharmacol*. 2004;14(1):11-28.
 31. Bloch MH, Qawasmi A. Omega-3 fatty acid supplementation for the treatment of children with attention-deficit/hyperactivity disorder

- symptomatology: systematic review and meta-analysis. *J Am Acad Child Adolesc Psychiatry*. 2011;50(10):991-1000.
32. Sonuga-Barke EJ, Brandeis D, Cortese S, et al. European ADHD Guidelines Group. Nonpharmacological interventions for ADHD: systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *Am J Psychiatry*. 2013;170(3):275-289.
 33. Pelsler LM, Frankena K, Toorman J, et al. Effects of a restricted elimination diet on the behaviour of children with attention-deficit hyperactivity disorder (INCA study): a randomised controlled trial. *Lancet*. 2011;377(9764):494-503.
 34. Graf WD, Nagel SK, Epstein LG, Miller G, Nass R, Lariviere D. Pediatric neuroenhancement: ethical, legal, social, and neurodevelopmental implications. *Neurology*. 2013;80:1251-1260.
 35. French WP, Kisicki MD. Management of disruptive disorders. *Pediatr Ann*. 2011;40(11):563-568.
 36. Steiner H, Remsing L; Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with oppositional defiant disorder. *J Am Acad Child Adolesc Psychiatry*. 2007;46(1):126-141.

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