Behavioral disorders in pediatric patients—primarily attention deficit hyperactivity disorder (ADHD)—pose a clinical challenge for health care providers to accurately assess, diagnose, and treat. In 2013, updated diagnostic criteria for behavioral disorders were published, including ADHD and a new diagnostic entity: disruptive mood dysregulation disorder. Revised criteria for ADHD includes oldest age for occurrence of symptoms, need for symptoms to be present in more than one setting, and requirement for number of symptoms in those aged 17 and older. Assessment of ADHD relies primarily on the clinical interview, including the medical and social history, along with the aid of objective measures. The clinical course of ADHD is chronic with symptom onset occurring well before adolescence. Most patients have symptoms that continue into adolescence, and some into adulthood. Many patients with ADHD have comorbid disorders such as depression, disruptive behavior disorders, or substance abuse, which need to be addressed first in the treatment plan. Treatment of ADHD relies on a combination of psychopharmacologic, academic, and behavioral interventions, which produce response rates up to 80%.

Revised criteria
Impairment before age 12 instead of age 6. As a neurodevelopmental disorder, ADHD usually starts at a young age; teenagers presenting with newly developed ADHD-type symptoms probably do not have ADHD and efforts should be made to rule out other illnesses or social dynamics. The DSM-5 raised the age limit for onset of qualifying symptoms to before 12 years (previously by age 6) primarily to capture a cohort of pediatric patients, typically female, who present solely with inattention symptoms and may not display overt functional impairment early on.

Symptoms required in at least two settings. Symptoms must be present in at least two settings to qualify for a diagnosis of ADHD. This ensures that the behaviors occur globally; they do not occur just at school or at home but occur in both places.

Fewer symptoms required for diagnosis in adolescents.

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Although the diagnostic criteria retain the same symptoms as those in DSM-IV for different age groups, individuals aged 17 and older are now required to display only five or more inattentive or hyperactive-impulsive symptoms. Previously, at least six were required.

Partial remission criteria
The concept of partial remission was introduced in DSM-5. This acknowledges that two-thirds of children diagnosed with ADHD do not have symptoms that functionally impact activities of daily living beyond age 18.

Oppositional defiant disorder
In DSM-5, oppositional defiant disorder (ODD) is defined by emotional and behavioral symptoms grouped into three categories:
- Constant anger or irritability
- Argumentative or defiant behavior (arguing with authority figures)
- Vindictiveness.

Because defiant behavior may represent difficulty with self-control, ODD is associated with executive functioning deficits that are present in ADHD. Children with ODD tend to perform best in situations in which they can dominate or exert authority. To qualify as ODD, the pattern of behavior must be consistent for longer than 6 months. A severity rating was added based on pervasiveness of ODD symptoms. Otherwise the diagnosis did not change.

Conduct disorder: Purposeful aggression
The hallmarks of conduct disorder are purposeful aggression (eg, bullying), destruction of property, deceitfulness or theft, and serious violation of rules (eg, running away from home, repeat truancy). Some consider conduct disorder to be a separate illness from ODD, whereas others consider it a continuum of the same disorder. Conduct disorder can manifest as violence, as in initiating physical fights, or it can manifest in behaviors such as truancy, stealing, lying, and running away from home without the physical-aggression aspect.

Intermittent explosive disorder
Failure to control aggressive impulses defines intermittent explosive disorder (IED). The aggressive outbursts can be verbal or behavioral and tend to be impulsive. A small subset of children display isolated aggression out of proportion to provocation. The disorder tends to manifest at ages 3 or 4, and a diagnosis requires a stable environment with no significant early childhood trauma. Most often these symptoms are seen in children with intellectual disabilities or an autism spectrum disorder.

Disruptive mood dysregulation disorder
A new diagnostic category in DSM-5 is termed disruptive mood dysregulation disorder (DMDD). This captures many children who previously would have been diagnosed with pediatric bipolar disorder, even though most of them do not fulfill criteria for bipolar disorder as adults. The presence of baseline irritability separates this disorder from IED, which requires intermittent rapid and severe outbursts. The severe temper outbursts of DMDD must be recurrent, with an average of three occurrences per week, and have background irritability. The symptoms must have a duration of at least 12 months and be present in two settings. A diagnosis of DMDD cannot be made earlier than age 6, with onset before age 10.

ASSESSMENT OF ADHD
The clinical interview in conjunction with objective scales is the primary tool for diagnosing ADHD. The most frequent source of information is from the parents followed by the child's schoolteachers. Patient interview, although unreliable in young children, should also be part of the assessment. Comparing the patient's functional impairment against children of a similar age is necessary for an ADHD diagnosis.

The medical history can help rule out children with asthma or allergy being treated with corticosteroids and those with hypothyroidism and hyperthyroidism whose symptoms often fulfill the diagnostic criteria for ADHD. Symptoms of ADHD also may appear suddenly after a traumatic brain injury or other neurologic event. Other psychiatric illnesses, especially learning disorders, mood disorders, anxiety, other disruptive behavior disorders, or substance abuse, can mimic ADHD.

Ruling out other factors from a social history (eg, family conflict, bullying, sleep deprivation, being overscheduled with activities) adds to the reliability of an ADHD diagnosis. For example, repetitive uprooting and frequent changes in schools can cause academic problems that may be mistaken for ADHD, and use of stimulants may have failed to improve symptoms in these children.

Assessment scales
Pediatric assessment scales that can be performed in an office are more practical than standardized clinical assessments (Table 1). The Vanderbilt ADHD Diagnostic Teacher Rating Scale correlates highly with a
diagnosis of ADHD. We use the Vanderbilt ADHD Diagnostic Parent Rating Scale for children up to age 1 year. Other scales track symptoms and functional impairment over time and can be administered before the patient’s appointment. The Conners Third Edition scale can be used to establish a baseline before initiating therapy and to help monitor changes over time.

Standardized tests to bolster the utility of the clinical interview include the Diagnostic Interview Schedule for Children and Adolescents and the Schedule for Affective Disorders and Schizophrenia in School-Age Children–Present and Lifetime Version. Free training is available regarding use of some of these standardized tests.

Developmental course, risk factors
The clinical course of ADHD is chronic. The onset of hyperactivity usually occurs at age 3 or 4, with combined hyperactivity and inattention usually appearing from ages 5 to 8.6 The evolution of symptoms is progressive and constant. Between 50% and 80% have symptoms that continue into adolescence, and in about 40%, symptoms continue into adulthood.7,8 Some children with ADHD have a temperament-neuropsychological profile characterized by aggressiveness, irritability, and mood lability. Deficits in planning, delayed aversion, and temporal processing are present.

Risk factors include prematurity, prenatal complications, an anoxic event, nutritional deficits (specifically iron and zinc), and lack of appropriate socialization.9-11 The disorder is heritable, which is usually clear from the clinical interview. Rates of delinquency and peer rejection are high. This may result in secondary comorbidity such as emotional, disruptive, or substance abuse problems.

Management strategies
Stimulants
The first-line pharmacologic treatment of ADHD is stimulants: methylphenidate, dexmethylphenidate, mixed amphetamine salts, dextroamphetamine, and lisdexamfetamine. Head-to-head trials of medications versus behavioral management favor medication use, even over the long term.12-14

Methylphenidate and amphetamines are equally effective and have similar adverse effect profiles. Insomnia and anorexia are the most common side effects of stimulants. Cardiac effects include tachycardia, chest pain, and hypertension. Very rarely, stimulants have been associated with sudden cardiac death syndrome in patients with underlying cardiac problems. The consensus is that stimulants are safe in the general population. The need to obtain an electrocardiogram before initiating a stimulant was removed by the US Food and Drug Administration (FDA) unless it is otherwise indicated.15

The response rate to stimulants is in the range of 70%. About one-third of patients have side effects, and approximately 15% have side effects severe enough to requiring changing or withdrawing the medication.16,17

Stimulants are available in several delivery systems. For the best effect, medications should be combined with behavioral management.
Alternatives to stimulants
If stimulants are ineffective, atomoxetine can be used to treat patients with inattention; however, its effect on hyperactivity and impulsivity is less pronounced than that of stimulants. Bupropion is another option for inattention. Both agents are well tolerated. Irritability and insomnia are side effects of atomoxetine, and liver damage is possible, so liver function tests must be ordered if the patient complains of upper-right-quadrant pain.

The evidence to support the use of modafinil is equivocal. Unlike stimulants, modafinil is associated with a slight increase in motivation. Alpha-2 agonists are effective for treating aggression in the setting of ADHD, especially in younger children, and are well tolerated. Extended-release forms are available.

Combination therapy
Polypharmacy is sometimes indicated in the treatment of ADHD. A stimulant used in combination with atomoxetine was shown to be superior to either treatment alone in improving symptoms of hyperactivity and inattention. The combination, however, markedly increased the incidence of appetite loss, insomnia, and irritability.

A more promising combination is a stimulant with an alpha agonist. Symptoms of hyperactivity and inattention were improved more with this combination than with a stimulant plus placebo, with no difference in side effects.

ADHD with comorbidities
Patients with ADHD, both adults and children, often have comorbid externalizing disorders and other emotional disorders, such as depression and anxiety, occurring in up to half of cases. These comorbidities are important to consider when developing a treatment strategy. The following describes treatment options for the most common ADHD comorbidities (Table 3).

**ODD or conduct disorder.** The first-line therapy for these patients is a stimulant plus behavioral therapy. Adding an alpha agonist to this combination may be indicated if the comorbidity is severe. Second-generation antipsychotics also have been used as add-ons to stimulants with behavioral therapy, but weight gain and hormonal side effects are common.

Behavioral interventions are effective in targeting disruptive behavioral disorders, specifically multisystemic therapy. Multisystemic therapy is intensive

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Rates</th>
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<tbody>
<tr>
<td>Oppositional defiant disorder</td>
<td>54%–67%</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>26%</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>20%–30%</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>12%–24%</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>10%–40%</td>
</tr>
<tr>
<td>Tic disorders</td>
<td>18%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3 Summary of drug therapy options for ADHD with comorbidities</th>
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<tbody>
<tr>
<td><strong>ADHD + oppositional defiant disorder or conduct disorder</strong></td>
</tr>
<tr>
<td>Stimulant or atomoxetine plus behavioral therapy</td>
</tr>
<tr>
<td>Stimulants + behavioral therapy + alpha agonist</td>
</tr>
<tr>
<td>Stimulants + behavioral therapy + second-generation antipsychotic</td>
</tr>
<tr>
<td><strong>ADHD + mood disorders</strong></td>
</tr>
<tr>
<td>Bipolar disorder</td>
</tr>
<tr>
<td>Second-generation antipsychotic; then add stimulant</td>
</tr>
<tr>
<td>Atomoxetine, alpha agonist, or bupropion</td>
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<tr>
<td>Major depressive disorder</td>
</tr>
<tr>
<td>Bupropion; then add stimulant</td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitor + stimulant</td>
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<tr>
<td>Cognitive behavior therapy + atomoxetine + alpha agonist</td>
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<tr>
<td><strong>ADHD + substance abuse</strong></td>
</tr>
<tr>
<td>Atomoxetine</td>
</tr>
<tr>
<td>Bupropion</td>
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<tr>
<td>Alpha agonist</td>
</tr>
<tr>
<td>Stimulant difficult to abuse (eg, lisdexamfetamine)</td>
</tr>
<tr>
<td><strong>ADHD + anxiety</strong></td>
</tr>
<tr>
<td>Atomoxetine</td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitor + stimulant or alpha agonist</td>
</tr>
<tr>
<td>+ cognitive therapy</td>
</tr>
<tr>
<td>Tricyclic antidepressants (for pediatric anxiety)</td>
</tr>
<tr>
<td><strong>ADHD + tics</strong></td>
</tr>
<tr>
<td>Alpha-2 antagonists</td>
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<tr>
<td>Atomoxetine</td>
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</tbody>
</table>
therapy that involves working with the patient’s peer group or school, but most children must enter the legal system to receive this intervention. Multisystemic therapy is the only intervention shown to improve symptoms associated with comorbid ADHD and conduct disorder.

Mood disorders. For these patients, the mood disorder is treated first. In doing so, symptoms of ADHD may disappear. For those with bipolar disease, a second-generation antipsychotic agent is superior to lithium in efficacy, maintenance of remission, and side effects in patients with a clear bipolar affective disorder, after which a stimulant can be added with less risk of developing manic symptoms. Using a stimulant first for this indication risks mood destabilization.

For patients with a major depressive disorder, bupropion can be used, although this indication is not FDA-approved, followed by the addition of a stimulant. One alternative is a selective serotonin reuptake inhibitor plus a stimulant; another is cognitive behavioral therapy plus atomoxetine and an alpha agonist.

Substance abuse. Patients with ADHD have high rates of substance abuse. Whether treatment of ADHD with stimulants reduces the risk of substance abuse is controversial. Because abuse of stimulants is common, start treatment with atomoxetine, bupropion, an alpha agonist, or a stimulant that is difficult to abuse (eg, lisdexamfetamine). Refer patients who are abusing substances to a specialist in substance abuse for behavioral management.

Anxiety. Atomoxetine is recommended for the treatment of anxiety that coexists with ADHD. A selective serotonin reuptake inhibitor in combination with a stimulant or alpha agonist, plus cognitive behavioral therapy, is another option for treating anxiety and ADHD. Tricyclic antidepressants have shown benefit in pediatric anxiety. Bupropion should not be used to target anxiety as it has been shown to have a limited effect on anxiety.

Tics. Stimulants may transiently exacerbate underlying tic disorders, but no longstanding difference in the course of tics has been observed with stimulant use. Alpha-2 antagonists target both tics and ADHD, so their use is preferred. Atomoxetine does not exacerbate tics but may reduce their frequency and severity.

Dietary factors
Although challenging to accomplish, management of diet, specifically removal of artificial food coloring and sodium benzoate preservatives, has been more efficacious than behavioral management in the long-term reduction of core symptoms of ADHD. No herbal remedy has demonstrated efficacy in improving ADHD symptoms. The use of omega-3 fatty acids as a complement to stimulants has demonstrated efficacy in reducing core symptoms in ADHD.

Behavioral therapy
Several forms of behavioral therapy have shown utility in improving symptoms in ADHD. Evidence supports that ADHD responds to cognitive behavioral therapy. In-school neurofeedback training for ADHD was shown to be better than cognitive training in improving inattention and hyperactivity-impulsivity at 6 months of follow-up.

Parental training has the most evidence to support its use in children with ADHD. The two most common forms are Pathways Triple P (Positive Parenting Program) and The Incredible Years. Triple P is an early intervention designed to promote positive parent-child relationships to reduce behavior problems. The Incredible Years is a multicomponent program that emphasizes creating opportunities for active involvement, reinforcement of positive behavior, teaching skills, and setting clear limits, all of which are central to the social development strategy.

Many children with ADHD respond to in-school interventions, at least an evaluation to rule out learning disorders, which typically have high morbidity. Children may qualify for Individualized Education Program (IEP) services, such as peer tutoring, computer-assisted instruction, and task-modification instruction. All of these have evidence to support their use.

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