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Treatment of Attention-Deficit/Hyperactivity Disorder: Summary of 2011 American Academy of Pediatrics Guidelines

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a frequently occurring psychiatric disorder that causes considerable suffering in patients and their families. It typically begins in early childhood, and a recent epidemiologic survey placed the prevalence of ADHD at 8.7% in children.[1] The incidence tends to be higher in boys than in girls, although percentages vary across studies. ADHD was initially thought to abate in adolescence and adulthood; however, it is now considered to be a chronic condition.[2] Persistence into adulthood may occur in up to 70% of those diagnosed in childhood[3] and epidemiologic studies have found the prevalence in adults to be over 4%.[4,5] If left untreated, ADHD can have serious consequences on an individuals ability to function as well as their health and well-being.

In October 2011 a new ADHD treatment guideline was published by the American Academy of Pediatrics (AAP).[6,7] Previous AAP guidelines were published in 2000 and 2001 and addressed the diagnosis and evaluation of ADHD in children and the treatment of ADHD, respectively. The 2011 guideline addresses the diagnosis and treatment of ADHD in children 4 to 18 years of age, whereas previous guidelines focused on children 6 to 12 years of age.

Guideline / Treatment Overview[6,7]

- Any child 4 through 18 years of age who presents with academic or behavioral problems and symptoms of inattention, hyperactivity, or impulsivity should be evaluated for ADHD.
  - To make a diagnosis of ADHD, the clinician should determine that criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) have been met (including documentation of impairment in more than 1 major setting) and rule out any alternative causes of symptoms.
  - In the evaluation of a child for ADHD, the clinician should include assessments for other conditions that might coexist with ADHD, including emotional or behavioral (e.g., anxiety, depressive, oppositional defiant, and conduct disorders), developmental (e.g., learning and language disorders or other neurodevelopmental disorders), and physical (e.g., tics, sleep apnea) conditions.
  - In addition to expanding the age range for treatment of ADHD, the 2011 guideline also provides information about the diagnosis of problem-level concerns in children based on the Diagnostic and Statistical Manual for Primary Care (DSM-PC), Child and Adolescent Version. This information includes suggestions for treatment and care of children and families with problem-level concerns who do not meet the diagnostic criteria for ADHD.
- ADHD should be recognized as a chronic condition, and children and adolescents with ADHD should be recognized as children and youth with special health care needs. Management of children and youth with special health care needs should follow the principles of the chronic care model and the medical home principles.

- Both behavior therapy and medications have been demonstrated to reduce behaviors associated with ADHD and improve function in preschool-aged children, elementary school-aged children and adolescents.
  - Medications should be restricted to children and adolescents who meet the diagnostic criteria for ADHD.
  - Medications should be titrated to achieve maximum benefit with minimum adverse effects.

Treatment for Specific Patient Groups[6,7]

- For preschool-aged children (4 to 5 years of age):
  - Evidence-based parent- and/or teacher-administered behavior therapy should be prescribed as the first line of treatment.
    - A multisite study NIMH-funded study which of preschool-aged children with moderate-to-severe ADHD found that many experience improvements in symptoms with behavior therapy alone.[8]
  - Methylphenidate may be prescribed if the behavior interventions do not provide significant improvement, and there is moderate-to-severe continuing disturbance in the child's function.
    - There are concerns about the possible effects on growth during the rapid growth period, and there has been limited information about and experience with the effects of stimulant medication in children between the ages of 4 and 5 years.
    - Many young children with ADHD may still require medication to achieve maximum improvement, and medication is not contraindicated for this age group, but response is less than in school-age.
    - Maximum doses of methylphenidate have not been adequately studied.
  - Dextroamphetamine is the only medication approved by the FDA for the use in children younger than 6 years of age. However, because of insufficient evidence for its safety and efficacy in this age group, the 2011 guideline does not recommend the use of dextroamphetamine.
    - Most of the evidence for the safety and efficacy of treating preschool-aged children with stimulant medications has been with methylphenidate. Although the use of methylphenidate in this age group is off-label, methylphenidate is recommended if the behavior interventions do not provide significant improvement and there is moderate-to-severe continuing disturbance in the child's function.
  - Limited evidence and no FDA approval in this age group are available for atomoxetine (selective norepinephrine-reuptake inhibitor), and no evidence or approval for extended-release (ER) guanfacine or ER clonidine (selective α_2-adrenergic agonists) is available.
- For elementary school-aged children (6 to 11 years):
  - Evidence-based parent- and/or teacher-administered behavior therapy and/or FDA-approved medications for ADHD should be prescribed. Preferably, behavior therapy should be combined with medications if medications are indicated.
  - Evidence strongly supports the use of stimulant medications.
  - Evidence is sufficient but less strong for atomoxetine, ER guanfacine and ER clonidine (in that order).
- Adolescents (12 to 18 years):
  - Behavior therapy and FDA-approved ADHD medications with the adolescents' consent should be prescribed. Preferably, behavior therapy should be combined with medications.
  - Adolescents should be assessed for symptoms of substance abuse before beginning medication treatment for newly diagnosed ADHD. When substance use is identified, assessment when off the abusive substances should precede treatment for ADHD.
  - Diversion of ADHD medications is of more concern in adolescents than in younger populations. However, diversion may occur in any age group as family members or others may divert younger children's medications.
  - Prescribing medications with no abuse potential such as atomoxetine, ER guanfacine or ER clonidine should be considered if drug diversion is suspected. If stimulant medications are indicated and diversion is a concern, extended-release products with less abuse potential should be preferred.
  - Longer-acting or late-afternoon, short-acting medications may be helpful in symptom control for driving.

ADHD Medication Overview

- Stimulant medications are highly effective in reducing core symptoms of ADHD in most children. All approved stimulant medications are methylphenidate or amphetamine compounds.
  - They are the first choice for medication treatment
- Atomoxetine (selective norepinephrine-reuptake inhibitor), ER guanfacine and ER clonidine (selective α_2-adrenergic agonists) also reduce core symptoms.
  - Only ER guanfacine and ER clonidine are FDA-approved as adjunctive therapy with stimulant medications.
  - Evidence base that supports the use of stimulants is larger than that of atomoxetine, ER guanfacine and ER clonidine.
- Adverse effects of stimulants:
  - Most common: appetite loss, abdominal pain, headaches sleep disturbance, and nervousness.
  - Decrease in growth velocity: A persistent effect of stimulants on decreasing growth velocity was found in the Multimodal Therapy of ADHD (MTA), especially when children were on higher and more consistently administered doses.[9] The effects diminished by the third year of treatment, but there was no compensatory rebound effects. The diminished growth was in the range of 1 to 2 cm.
  - Uncommon but significant adverse effects include hallucinations, other psychotic symptoms, and cardiovascular effects including increased blood pressure and/or pulse, stroke, and myocardial infarction. Psychotic or manic symptoms may be exacerbated in those with pre-existing conditions and may be treatment-emergent even with no prior history.
  - Rare: sudden cardiac death. Conflicting evidence exists on whether stimulant medications increase the risk of sudden death. Accurate patient history should be documented to include specific cardiac symptoms and structural cardiac abnormalities.
  - Increased mood lability and dysphoria has been reported in preschool-aged children.
- Adverse effects of atomoxetine:
  - Somnolence and gastrointestinal tract symptoms (especially if the dosage is increased too rapidly), decrease in appetite, increase in suicidal thoughts (less common), and hepatitis (rare)
  - Atomoxetine has a black-box warning of the possibility of suicidal ideation when initiating medication management. If there are any concerns about suicidal ideation, further evaluation, reconsideration about the use of atomoxetine, and more frequent monitoring should be considered.
- Adverse effects of ER guanfacine and ER clonidine: somnolence, dry mouth, and nausea. Bradycardia, hypotension, and syncope are possible.

Individualization of Treatment[6]

History of cardiac symptoms and cardiac family history such as sudden death, and death at a young age from cardiac conditions should be obtained. Vital signs, cardiac physical examination, and family history should be obtained on all patients and further evaluation should be obtained based on clinical judgment. If a trial with one compound group is unsuccessful (poor efficacy or adverse effects), a trial on a medication from another group should be undertaken. If concern about possible abuse or diversion of the medication exists or there is a strong family preference for non-stimulant medications, an FDA-approved non-stimulant medication may be considered as the first choice.

West Virginia 2012 Preferred Drug List (PDL) Changes

The West Virginia Medicaid Preferred Drug List (PDL) changed on April 1, 2012. On that date Adderall XR® (amphetamine salt combination, extended-release) became a non-preferred agent. In order to avoid disruption of therapy during the school year, patients on Adderall XR® received prior authorizations to continue through June 30, 2012. For your reference, the preferred and non-preferred medications for ADHD are listed below, and the PDL can be accessed at:

www.dhhr.wv.gov/bms/Pharmacy/Pages/pdl.aspx.

- Amphetamines:
  - **Preferred:** amphetamine salt combination (generic Adderall), dextroamphetamine, Vyvanse
  - **Non-preferred:** Adderall, Adderall XR, amphetamine salt combination ER (generic Adderall XR), Desoxyn, Dexedrine, Dextrostat, methamphetamine, Procentra
- Non-amphetamines:
  - **Preferred:** Concerta, Daytrana, Focalin, Focalin XR, guanfacine, Intuniv, Metadate CD, methylphenidate, methylphenidate ER, Strattera
  - **Non-preferred:** dexmethylphenidate, Kapvay ER, Metadate ER, methylphenidate ER (generic Concerta), pemoline, Ritalin, Ritalin LA and Ritalin-SR

FDA Approved Medications for Attention-Deficit/Hyperactivity Disorder[7]

ADHD MEDICATIONS	
Stimulant Products*	
Amphetamine Products	**Methylphenidate Products**
• Mixed amphetamine salts† (Adderall®¶, Adderall XR®¶) • Dextroamphetamine† (Dexedrine®¶, Dexedrine® Spansule®¶, DextroStat®, LiQuadd™, ProCentra®) • Methamphetamine (Desoxyn®¶) • Lisdexamfetamine (Vyvanse®§)	• Methylphenidate† (Methylin®, Ritalin®¶) • Methylphenidate ER†-/sustained-release (Concerta®§, Metadate CD™§, Metadate ER™, Methylin® ER, Ritalin-SR®¶, Ritalin LA®) • Methylphenidate transdermal (Daytrana®§) • Dexmethylphenidate (Focalin®§¶, Focalin XR®§)
Non-Stimulant Products	
• Atomoxetine (Strattera®§) • Guanfacine ER (Intuniv®§) • Clonidine ER (Kapvay™)	

* All stimulant products are Schedule II (C-II) controlled substances.
† Generic immediate release (IR) Adderall, generic IR dextroamphetamine, generic methylphenidate IR and ER (not generic Concerta) are preferred on the PDL.
§ Preferred agents on the PDL; generic IR guanfacine is also preferred (not listed).
¶ Available in generic form

Conclusions

ADHD is the most common neurobiological disorder of children and adolescents. The 2011 AAP guideline for the diagnosis and treatment of ADHD summarizes the treatment options for a broader range of patients and provides an overview of FDA-approved medications for ADHD. The guideline recommends that every child or adolescent with signs or symptoms suggestive of ADHD should be evaluated for ADHD. Treatment options differ between age groups, but the main cornerstone of ADHD therapy is evidence-based behavior therapy combined with medication therapy. In preschool-aged children, behavior therapy is the first-line treatment, and methylphenidate should be reserved for children with moderate-to-severe symptoms. Children ranging in age 6 to 18 should preferably receive both behavior therapy and FDA-approved medications for ADHD. Stimulant medications are the first choice for medication treatment. However, ADHD medications should be reserved for those who meet the diagnostic criteria for ADHD. The initiative to adopt the chronic care model and the medical home principles for ADHD treatment recognizes that ADHD often persist into adulthood, and the available treatments are not curative but only address the symptoms and help improve daily function. The 2011 AAP guideline provides an evidence base for the diagnosis and treatment of ADHD, but the challenge still lies in how to sustain appropriate treatments and achieve successful long-term outcomes.

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